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KERATOSIS PILARIS.*

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KERATOSIS pilaris can be demonstrated over the posterior aspects of the upper arms, the external aspects of the thighs and over the buttocks in a proportion of the population.

Stannus (1945) reviewed 4,000 children of school age and found that keratosis pilaris was maximal at puberty and the next few years of adolescence, particularly among girls who were well grown and plump. He examined girls of 14 years and found the incidence of keratosis pilaris was up to 80%. The incidence fell to 20% at the most in adult women. Stannus noted an increase of keratosis pilaris in cold and wet seasons. The high incidence in plump girls may be due to the insulating effect of fat, shielding the skin from heat radiated by the underlying muscle. The effect of cold and damp on the development of keratosis pilaris in those predisposed to this condition indicates the vulnerability of the follicular wall to anoxaemia and to various deficiencies.

McCance and Barrett (1951) studied the effect of undernutrition on the skin of the inhabitants of Wuppertal after the war, and noted a general dryness, scaliness and keratosis pilaris. They found all grades of follicular change from simple follicular erection and minute follicular excrescences, to hard spiky projections from the follicles. The extensor aspects of the limbs were usually involved, but in the severest example, a young civilian prisoner, the entire body, save the hands, feet, face and penis, was affected. McCance and Barrett came to the conclusion that a deficiency of calories was responsible for the skin changes, for there was an adequate supply of vitamin C in the diet and the blood level of vitamin A was normal in their subjects.

However, the blood level of vitamin A may not necessarily correspond with the skin content and Griesemener *et al.* (1953) state that the utilization of vitamin A

* The Papers in this number by Drs. Forman, Gougerot and Duperrat, Bettley and Page, Touraine, Malkinson and Wells, Degos, Lyon, and Bolgert and Canivet, were read at the Franco-British Meeting in Paris on 13.v.54.

is depressed by a lowered calorie and protein intake. It seems probable that the diet of the undernourished people observed by McCance was low in protein and fats, and in this connection one may recall that keratosis pilaris has been observed in Cushing's disease where there is an excessive breakdown of protein and nitrogen loss (Thorne, 1953).

Frazier and Hu (1931) described keratosis pilaris, keratomalacia and squamous metaplasia of the mucocutaneous junctions and upper respiratory tract as due to a vitamin A deficiency. Numerous clinical and experimental studies on the relationship between keratosis pilaris and vitamin A deficiency have been recorded. Loewenthal (1933) described keratosis pilaris as a sign of vitamin A deficiency in natives of Tanganyika and cured the condition with vitamin A in vegetable or fish oils.

However, Ramalingaswami and Sinclair (1953) point out that long standing cases of coeliac disease, who were shown to be deficient of vitamin A by absorption curves and blood levels, showed no signs of follicular hyperkeratosis. The effect of a diet deficient in vitamin A and its precursor, carotene, in 20 men and 3 women was reported (M.R.C. report No. 264); the maximum period of the experiment was 23 months. In only one individual was there any change in the skin: A mild degree of keratosis pilaris had been noted at the beginning of the test; after 4 months of the vitamin A deficient diet the keratosis pilaris spread to the legs and scapular regions. It improved after dosing with vitamin A, but did not clear up.

Sullivan (1945) endeavoured to obtain evidence in the rat of squamous metaplasia provoked by vitamin A deficiency. He reduced the epithelium to one layer by a diet deficient in vitamin B₂ group and then withdrew vitamin A. Hyperkeratinization of the skin and hair follicles then occurred. He stated, however, that the follicular hyperkeratosis of Frazier's cases corresponded to the follicular lesions produced experimentally in the rat by fat deficiency.

Ramalingaswami and Sinclair (1953), working with rats, believed that with vitamin A deficiency the epidermis became thin with a follicular hyperkeratosis of loose horn. On the other hand, a fatty acid deficient diet increased the thickness of the epithelium and the follicles were dilated with a hard concentric horny thickening. They suggested that Frazier's cases corresponded to the changes produced by a diet deficient in fatty acids.

Frazier (1953) is not convinced of the validity of this comparison between the thick and thin epidermis of these two rat deficiencies as applied to the phrynodermia of man. His cases did not shew a marked thickening of the epidermis in relation to the hyperkeratotic follicles. In certain situations, there was a distinct atrophy of the epithelial part of the hair follicle where the process had been long enduring. Among his Chinese patients, the degree of saturation of the fatty acids was significantly more than in the blood of Western

patients. Frazier treated his patients with concentrates of vitamin A in very small amounts of oil, far too small to affect the iodine number of the fatty acids in the blood.

Fell and Mellanby (1953) have presented evidence of the ability of high concentrations of vitamin A to inhibit keratinization of chick embryo and mouse skin in tissue culture, and to convert chick epithelium to mucus-producing cells. Flesch (1953) showed that in the rabbit and the mouse vitamin A and its synthetic precursor Hydroxenin had a direct local and probably non-specific antikeratinizing effect on epidermal cells by virtue of the unsaturated double bonds in the molecule. These unsaturated compounds inactivated SH groups of protein and of the enzyme succinic dehydrogenase.

Deficiency of vitamin B₂ in pellagra has been observed to be associated with keratosis pilaris, which also occurs in scurvy and experimental vitamin C deficiency. In the volunteer group observed in Sheffield (M.R.C. report No. 280) keratosis pilaris developed in a significant number of the subjects after 3 to 5 months of deprivation of vitamin C. The keratosis pilaris of puberty and Cushing's disease have been mentioned, and follicular keratinization has been noted following the administration of ACTH. Thyroid deficiency may present with a generalized hyperkeratosis and follicular hyperkeratosis. This occurred in a girl of 16 years (Forman, 1951) who also had loss of hair on the head and increase of lanugo hair on the body. The vitamin A blood level was lowered and the blood carotene slightly increased. The keratosis pilaris improved promptly with thyroid medication, the last area to clear being under the brassière suggesting that persistence was due to pressure. It is probable that there is a masked hypothyroidism in Cushing's disease and in patients treated with ACTH, as measured by the uptake of radioactive iodine and the serum protein-bound iodine (Wolfson *et al.*, 1951).

Vilanova and Canadell (1949) refer to keratosis pilaris associated with hypothyroidism following thyroidectomy. They observed regression of the keratosis pilaris after the administration of 20,000 units of vitamin A a day. The signs and symptoms of thyroid insufficiency were not changed but were reversed when the vitamin A was replaced by 0.2 g. of dried thyroid daily.

An interesting and paradoxical keratosis pilaris in an adult female due to hypervitaminosis A was described by Sulzberger and Lazar (1951). She had taken 600,000 units of vitamin A a day for 18 months. Follicular hyperkeratosis was evident on the thigh and posterior aspects of the arms. The skin was dry, irritable and scaling; the hair had fallen from the scalp and eyebrows. The clinical picture suggested hypothyroidism and the authors discuss the experimental and clinical relationship between vitamin A blood levels and thyroid activity, suggesting that there is a balancing mechanism. Thus a high vitamin A blood level would inhibit the thyroid or may interfere with the pituitary thyrotropic hormone.

To sum up, the follicular epithelium in certain predisposed individuals reflects the vital effect of a lowered temperature, a lowered metabolism, and of vitamin and endocrine deficiencies on the rate of keratin production, and results in the formation of the follicular horny plug.

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THE NODULAR DERMAL ALLERGIDES OF GOUGEROT.

H. GOUGEROT AND B. DUPERRAT.

OVER a period of more than thirty years Professor H. Gougerot has studied a particular syndrome falling within the group of dermatitis nodularis necroticans and non-necroticans, the successive titles of which trace its evolution. It was first called "a chronic indeterminate septicaemia with endocarditis, characterized by small dermal nodules, erythemato-papular elements and purpura" (1933). Then, as the endocarditis was found to be an inconstant feature, "a chronic indeterminate septicaemia with the triple lesions of purpura, erythema multiforme and nodules" (1935). Then, the term "septicaemic" being at variance with the negative blood cultures, it became known as "*Maladie trisymptomatique*". Bureau and Degos, however, suggested that it should be called "*Maladie trisymptomatique de Gougerot*" to avoid confusion with the "trisynndrome" of Milian (1946). With the gradual acceptance of the term "allergide", the syndrome has become known finally as "Nodular dermal allergides" (1951).

To the six original cases of Gougerot, a considerable number have been added by his pupils, and by others in France and abroad (Zureick, Boncinelli, Sa' Penella, etc.). Cases are now so numerous that they are no longer published individually.

At the St. Louis Hospital we have become very familiar with the disease, the diagnosis of which is straightforward when one has seen the condition even only once before. Not only is this true clinically, but also histologically, and on several occasions we have recognized the condition by the section, without having seen the patient. That the condition is of topical interest is shown by certain recent articles, such as that of Ruiter (1953) who, under the name of "allergic arteriolitis", deals with exactly the same condition.

Clinical description.—The syndrome consists of an eruption made up of three associated lesions :

(i) Small round nodules, from two to seven millimetres in diameter, situated in the dermis and projecting from the surface, or at the junction of the dermis and the hypoderm and projecting less obviously or not at all ; hard, well-defined, without any surrounding oedema, and of a normal colour or perhaps with a slightly rosy tint.

(ii) Purpuric macules from 1 to 5 mm. in size, occasionally more.

(iii) Erythemato-papular elements from 2 to 10 mm., rarely up to 20 mm., which are in exceptional cases annular or circinate resembling erythema multiforme, or sometimes urticarial or erythemato-macular.

This eruption, occurring for the most part in adults, is scattered on all parts of the body including the face, but its site of predilection is on the legs where hundreds of lesions may sometimes occur. It evolves in separate attacks, clearing up in 15 to 60 days, leaving no trace.

The pleomorphism of the eruption is marked. Thus, to the original "tri-symptome" which we have just described, may be added the following variations :

"Monosymptome", consisting only of nodules.

"Bisymptome", nodules with purpura, or nodules with urticaria.

"Tetra-" or "pentasymptome", when the eruption has, in addition, bullae, necrotic ulcers and so on.

Moreover angiomas, angiokeratomas, hypodermic infiltrated lesions and other variations can also occur. All these lesions are relatively painless, sometimes completely so. Itching is inconstant.

Evolution.—This is characteristic. The attacks settle down completely—that is to say the elements clear up without leaving any scars except, obviously, when necrotic ulceration has occurred. Sometimes the attacks are associated with fever, fatigue, arthralgia, and headache. Despite this, the general health is good, although the attacks may recur for many years (more than thirty years in one of our original cases).

Prognosis.—The prognosis as to life is good and it may even be possible that it is more favourable when the cutaneous eruption is the more florid "as if the condition were a defence reaction of the skin".

Histology.—From a large collection of biopsies we have been able to make a detailed study of the histological changes. The abnormal findings occur particularly in the arterioles and capillaries. They consist of :

(i) A considerable *swelling* of the endothelium, the cells of which soon compress each other, obliterating the lumen of the vessel.

(ii) *Fibrinoid necrosis* of the perithelium, giving rise, around the vessel, to a sort of continuous cuff. This is pale pink in colour and rather hazy, with a fibrillary appearance but as though the fibrils had been wiped out. The cuff may be fairly wide.

(iii) *Inflammatory infiltrate.*—This not only lies around the area of fibrinoid necrosis but also extends into the surrounding zone. The infiltrate, for the most part, consists of polymorphs whose nuclei are sometimes intact and sometimes pyknotic. Nuclei may be seen lying alone and also a fine chromatin debris. These are found elsewhere only in certain mycoses and can be considered almost pathognomic of the present condition. Eosinophils are rare.

The anatomical lesions are considerably more diffuse than one would expect on clinical examination. In a large biopsy one can find, in a zone that is apparently healthy, quite marked vascular changes.

Differential diagnosis.—The differential diagnosis from purpura and erythema multiforme is based on the co-existence of nodules, but in monosymptomatic attacks of dermal allergides purpura or erythema may, of course, occur alone.

The itching purpura of Loewenthal (1954) is quite different. Acute disseminated lupus erythematosus and dermatomyositis also have quite different characteristics. Of more importance are :

(i) *Subacute bacterial endocarditis*. This is accompanied by streptococci in the blood. The cutaneous eruption is usually minimal. Without penicillin the patients die.

(ii) *Polyarteritis nodosa*. A systemic affection, the visceral manifestations often presenting.

The prognosis of nodular dermal allergides is quite different from that of the last two conditions.

(3) Finally, the *Granulomatous vascular allergides* of Strauss, Churg and Zak. Their position is still uncertain. The combination of general symptoms, multiple visceral manifestations, and a blood eosinophilia, go hand in hand with a prognosis that is generally grave.

AETIOLOGY.

The mitral endocarditis that was found in the first three cases has not been observed since ; it was probably coincidental and, like the joint pains, a result and not a cause of the condition. Despite every effort, all investigations have been negative ; blood cultures, inoculations from blood, from purpuric spots and from nodules. We have sometimes found focal sepsis, such as sinusitis, dental abscesses, gall-stones, or amoebic dysentery ; and, in certain patients, a marked sensitivity to tuberculin or to staphylococcal or streptococcal antigen. Finally, the precipitating role of some therapeutic agents such as sulphonamides must be borne in mind.

Pathogenesis.—Although the aetiology often remains unknown, from a pathogenetic point of view the mechanism is an allergic one. Emboli of some microorganism or other, arriving at the skin, provoke a reaction which produces nodules if they are arrested in the mid or deep dermis, and papular erythema if in the superficial dermis. This is because the soil is sensitized against this particular organism. The lesion is witness of the battle and the destruction of the germs. And Gougerot adds : “ It is a cutaneous defence reaction which seems to come about as though to provide—I even dare say cause—the highest degree of defence, and thus insure the benign nature of the attack.”

The role of the endocrine glands deserves mention. Much experimental work, for instance that of Halpern, has stressed the role of the suprarenal glands in the regulation of capillary permeability. Roskam, studying a number of

cases of allergic purpura or nodular vasculitis has been able to observe a very irregular excretion of the 17-ketosteroids. No doubt further investigations of the pathology of nodular dermal allergides should be directed along these channels.

Classification of the eruption.—Without doubt this disorder should be classified within the immense group of cutaneous allergides, close to other nodular allergides, such as dermatitis nodularis necroticans of foreign authors, erythema nodosum, granuloma annulare, and rheumatic nodules.

The same allergic background is found in other dermatoses, such as the tuberculides, whose pleomorphism has been pointed out by Gougerot, Burnier and Eliascheff (papular, nodular, bullous, purpuric, necrotic and ulcerating forms); and among certain varieties of parapsoriasis varioliformis, necrotic pyodermites, etc.

The condition is the mildest form of cutaneous allergic disorder, of which polyarteritis nodosa is the most severe and lethal type and of which the granulomatous vascular allergides of Strauss, Churg and Zak are a fairly serious variety.

TREATMENT.

The aetiology may be so variable that many forms of therapy have been tried, depending on the cause in each patient. Vaccines, antitoxins, bacteriophage, sulphonamides, penicillin, and the like. Successes have been infrequent; now with sulphonamides, now with penicillin.

On the other hand, many cases of monosymptom and bisymptom have been cured by methylic antigen, and one other by a biopsy. But these successful issues are rare: there is no constantly helpful treatment. Perhaps one might try the extirpation of focal sepsis.

Despite the type of pathological changes present, no success has attended all manoeuvres of desensitization or antihistaminic therapy. Treatment with cortisone and ACTH merits a trial. We have not had sufficient experience of this to comment on it.

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THE EFFECT OF MEPACRINE ON LIGHT SENSITIVITY IN LUPUS ERYTHEMATOSUS.

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WHEN Page (1951) recorded the beneficial effects of mepacrine in the treatment of chronic fixed lupus erythematosus he suggested that this might result from (a) a cortisone-like effect of mepacrine ; (b) an increase of light tolerance produced by mepacrine or (c) an antagonism between mepacrine and adenosine triphosphate. Of these possible explanations the first does not seem particularly likely since cortisone has little beneficial effect on chronic fixed lupus erythematosus ; and since mepacrine has not been shown to exert any of the physiological actions of cortisone or ACTH. The present investigation was, therefore, undertaken to test the second theory.

Patients with chronic fixed lupus erythematosus, hitherto untreated with mepacrine, were investigated without further selection. They were given mepacrine in doses varying up to 100 mg. twice daily and their sensitivity to light investigated monthly. An attempt was then made to correlate clinical improvement of the lupus erythematosus with alterations of light tolerance.

METHOD.

It was recognized that if an increased tolerance to light was responsible for clinical improvement the wave-lengths of light concerned must be those in the solar spectrum. It would, therefore, have been desirable to test light sensitivity with natural sunlight, but in London even in the summer this is so uncertain that it was decided to use a more reliable artificial source. A Hanovia Alpine sun lamp was chosen for the purpose. This mercury arc lamp, of course, produces considerable amounts of ultraviolet rays of shorter wave-lengths and biologically more active than those of natural sunlight. A filter of cellulose acetate was therefore interposed between the lamp and the skin, the action of which was to absorb all radiation below 2900Å. There is reason to believe that comparatively small variations in voltage may make an appreciable difference to the output of a mercury vapour lamp, so it was thought necessary to use a photo-

meter to ensure accuracy of dosage. The photometer chosen was an antimony-caesium photo-electric cell* suitably screened with a wire gauze grid. The cell when connected to a photometer† is designed to show maximum sensitivity to the ultra-violet and violet part of the spectrum.

Non-irradiated normal skin of the abdominal wall was used in testing. The abdomen was covered with a screen in which were twelve small openings that could be closed with shutters at varying intervals, usually of a quarter of a minute. The photo-electric cell was placed close to the skin to be tested, and the distance of the lamp adjusted to give a constant reading on the photometer. The skin was examined 8 and 24 hours afterwards and a note made of the minimum amount of irradiation required to produce erythema. This time, to the nearest quarter of a minute, was called the minimal erythema dose (M.E.D.).

Nine patients with chronic fixed lupus erythematosus were studied.

RESULTS.

Light Sensitivity in Untreated Lupus Erythematosus.

Of five control subjects the M.E.D. was found to be 7 minutes in three, and $6\frac{1}{2}$ and $7\frac{1}{2}$ minutes in the other two, average 7 minutes. Some of the lupus erythematosus patients tested had already received some mepacrine before the first M.E.D. was determined. In those who had not been treated the M.E.D. was $2\frac{3}{4}$, $3\frac{3}{4}$, $4\frac{1}{2}$, $1\frac{1}{2}$ and $5\frac{1}{2}$ minutes. It will be seen, therefore, that while there is considerably more variation in the light sensitivity of these patients than in the control subjects the average M.E.D. ($3\frac{3}{5}$ minutes) was approximately half that of the normal. In other words, these patients were about twice as sensitive to light.

Changes in M.E.D. after the Administration of Mepacrine.

Variations in M.E.D. during the course of mepacrine administration are set forth in the accompanying charts where the curve of light tolerance is superimposed on a chart of mepacrine dosage. It was found that in every patient the sensitivity of the skin as tested decreased after mepacrine had been given; very seldom, however, did the light tolerance reach normal.

Fig. 1 shows a typical effect; here the M.E.D. was $3\frac{3}{4}$ minutes before treatment was started. After one month of treatment it had risen only to 4 minutes but at the end of the second month it was up to $5\frac{3}{4}$ minutes. On a reduced dosage of mepacrine over the following four months this increased light tolerance was roughly maintained. Fig. 2 shows a similar effect in which the maximum tolerance was not reached until four months after beginning treatment. By this time the dose of mepacrine had already been considerably reduced to

* Cinema Television Ltd., Type QVA 39, A4208.

† Baldwin Instrument Company, Mark 3.

50 mg. daily. After a further four months the M.E.D. had still not returned to pre-treatment value although no mepacrine had been given for the past three months. Fig. 3 shows a comparable result; here the maximum light tolerance was reached after three months and had fallen off slightly by the seventh month on a reduced dosage. At the twelfth month, however, although no mepacrine

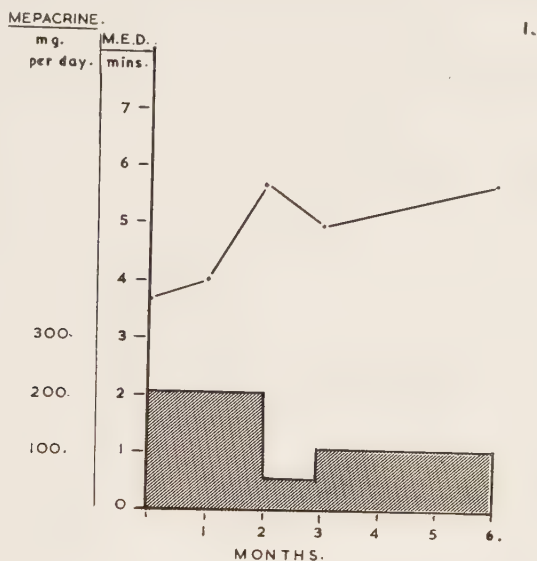


FIG. 1.—The shaded area represents mepacrine dosage and the linear curve the M.E.D.

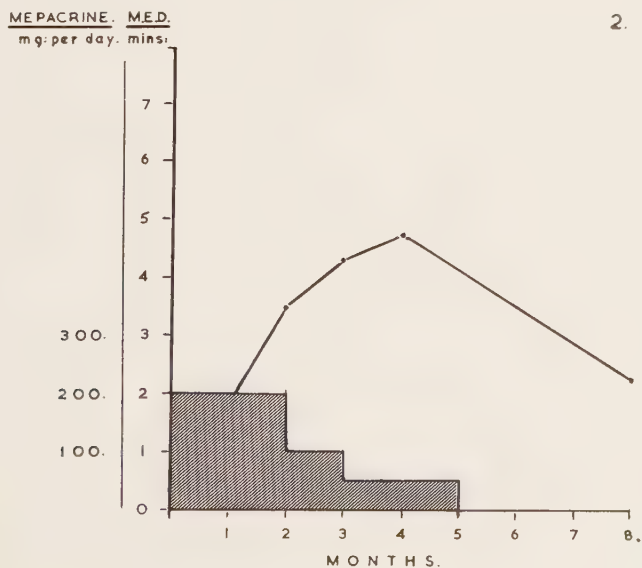


FIG. 2.

had then been given for four months, the M.E.D. was still above pre-treatment level.

The three above cases show a considerable delay between the start of administration of mepacrine and its effect on light tolerance. This effect was not,

3.

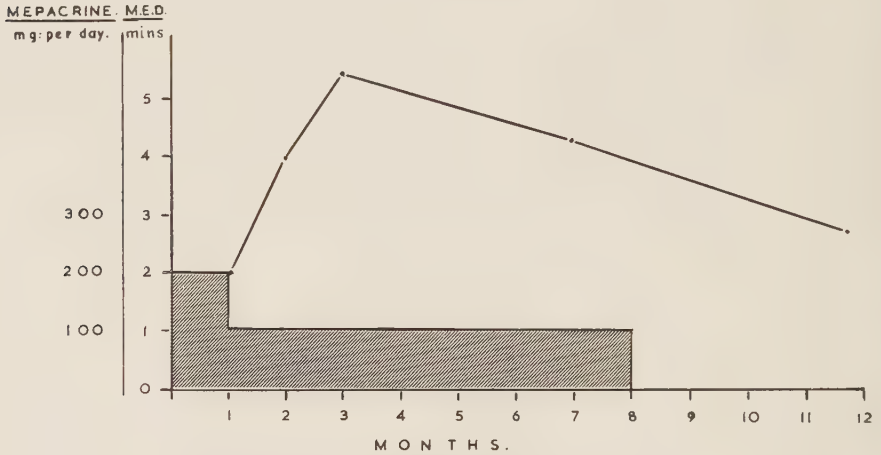


FIG. 3.

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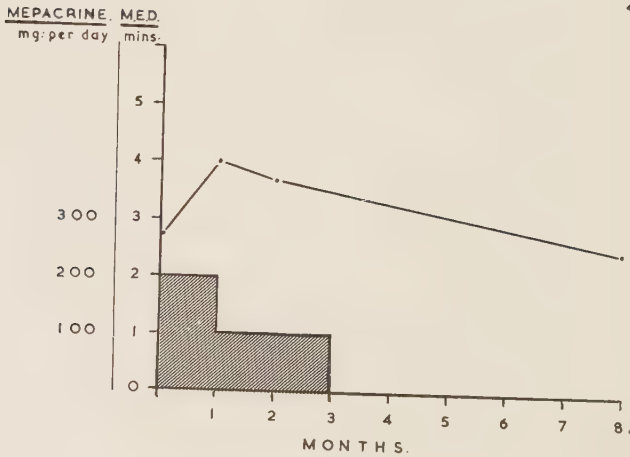


FIG. 4.

however, always shown. For example, Fig. 4 shows that in this case the highest tolerance was reached after only one month's treatment. This patient made good clinical progress and no treatment was given after three months. At the end of the ensuing five months it will be seen that the light tolerance had fallen to even below the pre-treatment level.

In summarizing these results we may say that in all the cases examined the administration of mepacrine increased light tolerance. The maximum tolerance achieved after treatment was, in most cases, at least 50% and sometimes over 100% greater than the pre-treatment level.

It is interesting and important also to observe that this increase in light tolerance usually follows mepacrine dosage with a lag of several weeks. The yellow coloration of the skin shows the same lag, suggesting that mepacrine is slowly deposited in the skin and accumulates over a period of several weeks. It will be observed also that reduction in dosage of mepacrine results in some return of light sensitivity also after a lapse of several weeks. Discoloration of the skin behaves in the same way, slowly disappearing when treatment is stopped. These results appear to indicate that the administration of mepacrine increases light tolerance and that this occurs concurrently with the gradual accumulation of mepacrine in the skin.

The Correlation of Clinical Improvement and Change in Light Tolerance.

Since clinical improvement is not susceptible of numerical evaluation the correlation between clinical improvement and increased tolerance to light is not so easy to demonstrate conclusively. Early observations (Page, 1951) suggested that clinical improvement appeared to go hand in hand with pigmentation of the skin and that the patients who became more yellow were those whose lupus erythematosus improved most. However, Black (1953) in a careful analysis concluded that mepacrine staining of the skin bore no relation to clinical improvement; nor did the total amount of mepacrine administered. In the cases which formed the subject of this report increase in light tolerance occurred constantly and clinical improvement of the skin was also observed in all of them.

The patient recorded in Fig. 1 showed already less induration after one month's treatment, although at this time the increase in M.E.D. of a quarter of a minute was so slight as to be negligible. At the end of the second month, when the M.E.D. had substantially increased, the patient was very yellow and a marked improvement in the skin was recorded.

In the second patient (Fig. 2), whose first test was only after one month's treatment, a marked clinical improvement was already recorded at that time although the M.E.D. was remarkably small. Clinical improvement continued over the months that followed, but did not appear to be particularly rapid about the third and fourth month when light tolerance was at its greatest.

Again, Fig. 3 records a patient who had already made great improvement after one month's treatment when the M.E.D. still stood at a very low figure.

Light tolerance tests were somewhat incomplete in the case recorded in Fig. 5. Considerable clinical improvement had already occurred by the end of the second month when the first M.E.D. was recorded. Improvement continued,

but at the end of the fourth month the condition became slightly active again although the M.E.D. had not fallen substantially. After another month there was further clinical improvement although by this time the M.E.D. had fallen and was the lowest hitherto recorded in that case.

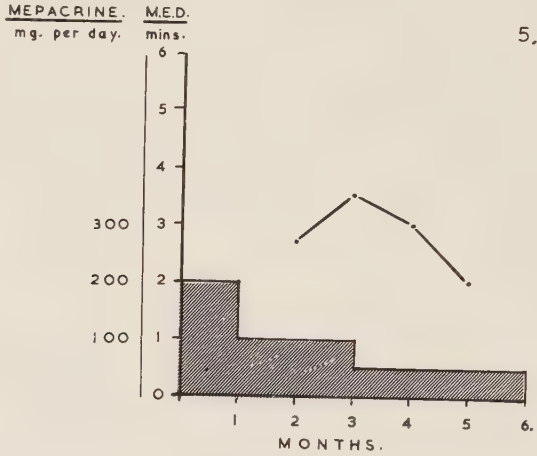


FIG. 5.

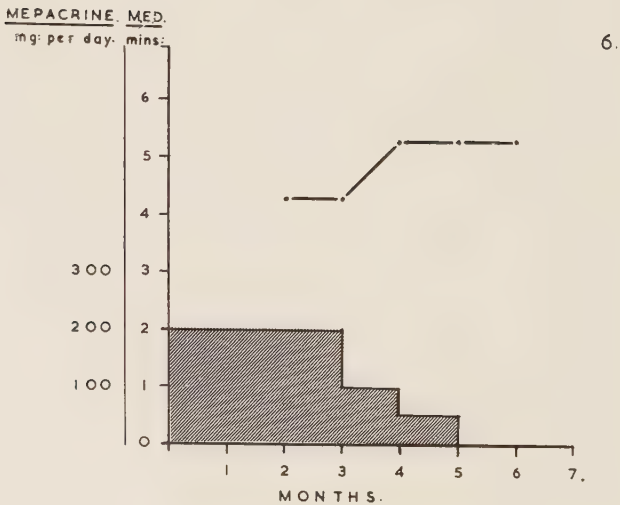


FIG. 6

A further observation of similar sort is seen in Fig. 6. In this case the M.E.D. was never very low; in the first four months considerable clinical improvement was recorded, and at the fifth month mepacrine was stopped. At the sixth month the skin lesions had started to relapse. In spite of this the M.E.D. had not altered.

These results appear to indicate, therefore, that while the increase in light tolerance is very gradual, the clinical effect on the lesions of lupus erythematosus occurs sooner. Some patients notice an improvement within a week of starting treatment. In all of these patients notable clinical improvement was observed after one month of treatment and the degree of improvement in the second and third months was no greater. When mepacrine dosage was reduced relapse was sometimes observed without a corresponding fall in M.E.D.

It is well known that sensitivity to light occurs in lupus erythematosus and may play a part in producing exacerbations. It seems likely that in some patients any factor that increases light tolerance will diminish the severity of lupus erythematosus. The experiments recorded here seem, however, to indicate that mepacrine has another action which exerts a more immediate effect on the disease itself than simply by increasing tolerance to sunlight.

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CONGENITAL POLYKERATOSIS.

A. TOURAINE.

UNDER this designation I am not describing a hitherto unpublished disease ; I am merely assembling, in a spirit of synthesis and in a unifying concept, various congenital anomalies usually considered as isolated and independent affections and often relatively widely separated in dermatological nosology.

Congenital polykeratosis, the essential feature of which is a tendency to overactivity of the process of keratinization, is a familial hereditary polydysplasia. It provides an example of those "genetic chains", produced by linkage of genes situated side-by-side in single chromosomes, of which I have on several occasions (1941, 1943, 1945) demonstrated the importance both in dermatology and in other fields of pathology. As in other examples, this chain may be present in the complete form and be transmitted in its entirety from one generation to another following the rules of regular dominant inheritance (sometimes irregular if there are "conductors"). More often the chain breaks up into shorter fragments, each containing a larger or smaller number of links, the number being sometimes reduced to one or two according to the fortuitous cross-over of premeiosis, during the formation of the gametes. The chain is transmitted, therefore, from one subject to another always as a dominant character, sometimes in the complete form, sometimes with alternation between its individual elements, and becomes either shorter or longer by the subtraction or addition of one or more links. Thus there are numerous incomplete or even monosymptomatic forms of this large polydysplasia. The essential nucleus of this congenital polykeratosis, which is never absent and which is its fundamental characteristic, is a tendency to hyperkeratinization of skin and mucous membranes, sometimes generalized to all or almost all of the skin, sometimes systematized according to a specific pattern, and sometimes localized to a restricted region. To the hyperkeratosis may be added dyskeratosis, though rarely in the same degree as in Darier's disease ; and quite often acantholysis also, shown by the formation of bullae as in epidermolysis bullosa.

Around this nucleus are customarily grouped other dysplasias of the skin and its appendages, such as erythemas, hyperidrosis, hyperpigmentation and abnormalities of hair and teeth. Others are yet more complex and are evidence of a more or less important participation of the whole organism in this disorder of cutaneous development : elements of the status dysraphicus, psychological

abnormalities (which justify the classification of polykeratosis with the neurodermo-ectodermoses), modifications of general resistance and biotrophy.

All the elements of the chain are congenital, stable since they are not progressive, and fixed; they are of hyperplastic type morphologically or functionally. Congenital polykeratosis is thus an example of that large class of congenital dysplasias which I have named the "hyperectodermoses".

ELEMENTS OF CONGENITAL POLYKERATOSIS.

Let us indicate in more detail the elements of this genetic chain :

1. *Mucocutaneous keratoses*.—The most constant, indeed seldom absent, is keratoderma or keratosis of the palms and soles (rarely purely plantar or palmar) with its diverse clinical manifestations :

—diffuse, of the Thost-Unna type, either as a sole thicker and smoother than normal or as a horny covering more or less dense or exuberant ;

—in streaks or bands (Brünauer-Fuhs type), with the rare mutilating variety resembling ainhum ;

—disseminate, punctate or papular (Büschke-Fischer or Brauer type), most common on the soles in islands, callosities, corns, keratomas, or keratotic horns, especially at points of pressure or occupational friction, and sometimes of the prokeratotic type of Mantoux.

(It must be clearly pointed out that the Meleda type of keratoderma of recessive inheritance does not form part of congenital polykeratosis.)

The following keratoses are also frequent :

Subungual hyperkeratoses, sometimes warty, isolated or more commonly co-existing with palmo-plantar keratosis or with pachyonychia.

Follicular keratoses, more or less constant, disseminated or grouped in small patches, plaques or sheets with more or less sharply defined borders, generally on the extensor surfaces of the limbs or on regions exposed to friction or pressure. They are either mild as in keratosis pilaris of the common type, or more accentuated as an acne, sometimes of comedo type; as grouped or isolated horny papules or even as a true lichen spinulosus; or in the form of the squamous type of follicular keratosis as described by Dohi of Japan. When sufficiently abundant and predominant the follicular keratosis, isolated or in erythemasquamous plaques, can present the clinical picture of pityriasis rubra pilaris.

Cutaneous keratoses.—These are sometimes mild and diffuse as in simple ichthyosis, sometimes more accentuated and widespread, producing the various forms of erythrokeratoderma or even of malignant keratoma. They may be locally exaggerated into horny plaques, especially in the region of the Achilles tendons and of the olecranon processes, or into verruciform papules as in epidermodysplasia verruciformis or acrokeratoma of Hopf, into papillo-

matous vegetations as in the severe forms of certain erythrokeratodermias, into the horny plugs of Kyrle's disease, or even into true cutaneous horns.

Keratosis of the mucous membranes affect particularly the mouth (the cheeks and more especially the dorsum of the tongue) in the form of leucokeratosis or a scaly leucoplasiform covering in spots, in bands or in a diffuse sheet, and may extend to the uvula and to the tonsils. This process may also involve the cornea (keratitis and even blindness) and, more rarely the lens (cataract), the lacrimal puncta, the olfactory membrane, the middle ear (hypoacusia, deafness), or the larynx (hoarseness of the voice).

2. *Other Systematized Hyperplasias.*

Hyperonychias : *Pachyonychchia* is the most common, especially on the fingers, with greatly thickened massive nails, with bevelled arciform free edges, usually resting on a heavy accumulation of subungual hyperkeratosis. *Onychogryphosis* is seen more often on the toes, with blackish masses of nail, hard and irregular and sometimes of enormous size. Rarer are *claw nails*, strikingly convex in their central portions and terminating in an elongated extremity curved back and pointed, and *Hippocratic* nails. Inflammatory episodes may lead to the temporary loss of one or more nails.

Erythema.—Exceptionally isolated, particularly on the palms (erythema palmare of Lane, after Schmidt-La Baume), this is usually seen beneath or immediately surrounding areas of keratosis, particularly as a border around sheets of palmo-plantar keratosis. It is the more visible, the thinner the keratosis through which it is seen, e.g. in dominant forms of hereditary ichthyosiform erythrodermia, and generalized or symmetrical keratodermias. It is sometimes subject to temporary congestive episodes (variable erythrokeratodermias).

Hyperidrosis, slight or marked, is rarely generalized but more or less constant on palmo-plantar keratoses ; it may occur also on the nose, the axillae, the groins, and the genital region. Sometimes it leads to the formation of small sweat-duct cysts.

Pemphigoid bullae, arising on normal skin, usually traumatic but sometimes apparently spontaneous, usually few and small, occur especially around the keratoses and provide a link with epidermolysis bullosa and with the benign familial pemphigus of Gougerot and Hailey-Hailey.

Hyperpigmentation.—These subjects are always of dark complexion with dark eyes. Moreover, it is not uncommon to discover spots or patches of hyperpigmentation either in the keratotic regions or on healthy skin at a distance from them.

Hair.—This is usually normal but may be exceptionally abundant and dark in colour. One often notes coalescence of the eyebrows and hyper-

trichosis of non-hairy parts. Keratosis pilaris may, however, produce atrophy of the hair whence results a hypotrichosis which has been known to involve not only the scalp but also other hairy regions.

Teeth.—These are normal or hyperplastic (teeth present at birth, rapid growth, large upper median incisors). One sees also abnormalities of implantation, fusions, and early caries.

Various other dysplasias, inconstant and accessory, may be seen : pigmented cellular and vascular naevi ; multiple lipomata of skin or intestines ; sebaceous cysts ; acanthosis nigricans ; hyperplasia of lips or gums ; large or scrotal tongue ; laxity of the joints ; hypercalcification of the skeleton ; Hippocratic fingers ; genital hypertrophy ; elements of dysraphism (bifid uvula, high palatine vault, oxycephaly, cranial asymmetry, enuresis, spina bifida occulta, etc.).

There may be a tendency to malignant change of warty cutaneous keratoses ; this may occur in epidermodysplasia verruciformis, acrokeratoma of Hopf and in erythrokeratoderma.

3. *Mental disturbances.*—One usually notes a more or less marked hyperthymia compatible, however, with a normal or above average intelligence. These subjects usually have a lively personality tending to dominate, sometimes with prolixity, pseudologia, excitability, turbulence, irascibility, or emotional instability ; and even occasionally epilepsy or its equivalents, kleptomania and schizophrenia.

4. *Expectation of life.*—This is almost always normal or above normal. Vigour, activity and a tendency to longevity confer on congenital polykeratosis a prognosis which is in general favourable both as regards life and function, although the skin lesion is stable and fixed with the exception of rare spontaneous regressions of certain elements in the long run or at about the time of puberty.

CLINICAL FORMS.

All the elements of congenital polykeratosis can exist in isolation or be associated in more or less complex combinations thus forming very many syndromes of which several have found a place in clinical terminology.

As *isolated elements* they thus appear, inherited as dominants, in the form either of one of the types of palmo-plantar keratosis or of pure pachyonychia, onychogryphosis, or sub-ungual hyperkeratosis ; of follicular or cutaneous keratoses (hence, for example, keratosis extremitatum hereditaria progrediens of Greither), or even as bullae (recurrent bullous eruption of the feet of Cockayne).

Much more often it is a matter of syndromes in which several elements are combined. Here are some examples among many :

Two elements : Palmo-plantar keratoderma may be associated with hyperidrosis of the same regions (very frequent in practice) ; or with pachyonychia (fairly frequent) ; or with follicular or cutaneous keratoses ; or with hypotrichosis : Pachyonychia or onychogryphosis with follicular keratoses. ichthyosis hystrix, with leukoplakia of the mucous membranes, or with drumstick fingers : Follicular keratoses with leukoplakia of the mucous membranes or with hypotrichosis.

Three elements : Palmo-plantar keratoderma may be seen with pachyonychia and buccal leukoplakia ; with hypotrichosis and Hippocratic fingers ; with follicular keratoses and leukoplakia of the mucous membranes ; with follicular keratoses and cutaneous and buccal bullae ; with palmo-plantar hyperidrosis and bullae ; with pachyonychia and buccal and olfactory leukoplakia ; with hyperidrosis and alopecia ; with bullae and premature loss of the teeth ; with ichthyosis bullosa and erythema of trunk and extremities ; or with ichthyosiform erythrokeratoderma and buccal leukoplakia. Similarly ichthyosiform erythrokeratoderma is linked with buccal leukoplakia and rapid growth of the teeth, or with hyperidrosis and buccal or ocular keratosis. Onychogryphosis may occur with alopecia and hyperidrosis, or with hyperpigmentation and oligophrenia or schizophrenia.

Four elements : Palmo-plantar keratosis may be combined with claw nails, cutaneous keratoses, and alopecias ; or with hyperidrosis, leukoplakia and alopecia of the lashes : Pachyonychia with hypotrichosis, Hippocratic fingers and imbecility. The following may be listed here ;

Jadassohn and Lewandowsky's syndrome : Palmo-plantar keratoses and hyperidrosis, with pachyonychia, follicular keratoses, lingual leukokeratosis, and granulosis rubra nasi.

Siemens's syndrome or keratosis multiformis : Punctate palmo-plantar keratoses with hyperidrosis, cutaneous keratoses either follicular or in plaques (of acneiform or comedo type), buccal leukoplakia and oligophrenia.

Schaefer's syndrome : Palmo-plantar keratoses and hyperidrosis, pachyonychia, cutaneous keratoses both follicular and in plaques, leukoplakia, cataract, oligophrenia, and hypotrichosis areata.

(Congenital dyskeratosis, as described by Engman and by Cole : Disseminated cutaneous keratoses, reticular pigmentation, atrophy of the skin of the hands as in acrodermatitis, palmo-plantar hyperidrosis, atrophy of the nails, buccal leukoplakia, and obliteration of the lacrimal puncta.

The syndrome of Kumer and Loos : Palmo-plantar and follicular keratoses with pachyonychia and callosities of the heels (type 1), sometimes with buccal leukokeratosis (type 2 or Riehl's type) or with keratitis (type 3).

The ectodermal syndrome of Hanhart : Disseminated palmo-plantar keratoses, cutaneous keratoses, multiple lipomata, sometimes keratitis, and imbecility.

CORRELATION.

Congenital polykeratosis, an hereditary polydysplastic chain of which I have just summarized the elements and the clinical forms, constitutes an entity of which hyperkeratosis is the characteristic feature to which may be added a local or general process of structural or functional hyperplasia.

With the hyperkeratoses are sometimes associated, in all degrees and in multiple combinations, other abnormal histological processes which may be of fundamental importance in other polydysplasias and thus establish all stages of transition between them. Let us indicate here the more important of these.

Atrophy of the stratum mucosum of Malpighi and of the subcutaneous fat, with slight hyperkeratosis—changes which characterize various types of ichthyosis and which, when the hyperkeratosis is more marked, constitute the states of nacreous, serpentine ichthyosis and ichthyosis hystrix. Added erythema characterizes certain ichthyosiform keratodermias. These various dysplasias may on the other hand include elements of congenital polykeratosis.

Dyskeratosis is rarely important in polykeratosis. It manifests itself, as accessory and isolated elements, in thick-walled segregated cells or in the *corps ronds* of Darier's disease and epidermodysplasia verruciformis. Here again these two affections comprise an important degree of hyperkeratosis (palmo-plantar keratoses, follicular keratoses), pachyonychia and pigmentary abnormalities, as in polykeratosis.

Acantholysis results in the formation of bullae which, by their frequency and their recurrence, become the principal elements of epidermolysis bullosa in both its simple and hyperplastic forms. These subjects often show a tendency to hyperkeratosis, and the same is true of benign familial pemphigus.

Although these diverse abnormalities of the epidermis may be only incidental and of little importance in congenital polykeratosis they none the less provide further evidence of the interdependence and of the unity governing every detail of the development of the skin as in the rest of the organism.

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CLINICAL EXPERIENCE WITH HYDROCORTISONE OINTMENT.

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EARLY reports on the effectiveness of hydrocortisone (compound F) ointment as a topical application have been somewhat contradictory. Goldman and Preston (1953) reported negative results from the use of hydrocortisone ointment in many common dermatoses but remarked upon its striking effect in resolving granuloma pyogenicum. Sulzberger, Witten and Smith (1953) reported good results with the ointment in 20 of 30 cases of atopic dermatitis. The effect of hydrocortisone ointment is confined to the area of application and there is no systemic effect, as judged by the circulating eosinophil counts, even when large inunctions (6 g.) of the 2.5% ointment are used (Smith, 1953). As the free alcohol is more effective than the acetate of hydrocortisone when taken by mouth, the former was incorporated in an ointment base and compared with the acetate, but no appreciable difference could be detected between their topical effects (Sulzberger and Witten, 1953).

During the past 18 months we have observed the effect of hydrocortisone ointment* on various superficial inflammatory dermatoses in 71 patients at the University of Chicago Clinics : 2.5% hydrocortisone acetate in a base of liquid paraffin, petrolatum, cholesterol and multiwax was applied very thinly to the affected areas of the skin three times daily. Wherever possible comparison was made between similar lesions on opposite sides of the body, one side receiving hydrocortisone ointment and the other the ointment base alone. It was instructive to see how often the ointment base alone gave an improvement equal to that of the hydrocortisone ointment, and in these cases the results were regarded as negative although both sides improved. By a good response is meant a definite improvement compared with the ointment base, though the result was not necessarily better than that which might be produced with other effective topical therapy. An excellent response implies an effect better than that obtainable with any other measures.

Of 17 cases of atopic dermatitis (including 8 cases of infantile eczema), 9 showed a good response and in 8 there was no effect.

Of 9 cases of chronic neurodermatitis in adults (including lichen simplex chronicus and exudative neurodermatitis) 3 showed an excellent response, 4 showed a good response and in 2 there was no effect.

* The hydrocortisone ointment was supplied by the Upjohn Company, Kalamazoo, Michigan.

Of 12 cases of contact and other eczematous dermatitis, 7 showed a good response and in 5 there was no effect.

Of 9 cases of seborrhoeic dermatitis, 1 showed an excellent response, 4 showed a good response and in 4 there was no effect.

Of 3 cases of nummular eczema, 2 showed a good response and in 1 there was no effect.

Of 5 cases of pruritus ani, 3 showed an excellent response and in 2 there was no effect.

Of 3 cases of eczematous dermatitis of the eyelids all showed a good response.

Of 7 cases of chronic itching otitis externa, 4 showed an excellent response and 3 showed a good response.

Entirely negative results were seen in generalized exfoliative dermatitis (2 cases), in psoriasis vulgaris (2 cases), in pemphigus vulgaris (1 case), in chronic discoid lupus erythematosus (1 case) and in autosensitization and "id" eruptions (1 of each).

In 4 of the 71 patients treated the ointment seemed to irritate and was discontinued, but allergic sensitivity to hydrocortisone was not demonstrated.

One of our patients developed an acute paronychia while the hand was being treated with hydrocortisone ointment. In two cases of eczematous dermatitis in which there was secondary staphylococcal infection, hydrocortisone improved the dermatitis without any worsening of the infection. Evidently more observations will be needed before it can be decided whether topical therapy with hydrocortisone favours superficial infection, since the factors involved in systemic steroid therapy may very well be different.

In many of these cases a good response implied a positive effect of the hydrocortisone beyond that seen with the ointment base, while not necessarily indicating a result superior to that which might be obtained with other local applications such as ichthyol or tar. In 11 of our cases, however, hydrocortisone seemed to offer more relief than any other treatment. Pruritic eczematous lesions in certain regions of the body (the eyelids, the pinna and especially the area around the external auditory meatus, and the anal and genital regions) respond particularly well to hydrocortisone ointment; and these are areas where other local applications are often poorly tolerated and where itching is particularly distressing. A patient with neurodermatitis disseminata after some months' experience with compound F ointment and other applications, is inclined to use less costly applications such as coal tar ointment on most areas, reserving the hydrocortisone ointment for use on the face or in the genital region.

In spite of prolonged suppression of symptoms, withdrawal of hydrocortisone ointment is followed by relapse in most chronic cases. A typical good response illustrates this point: A 36-year-old man had had pruritus ani for 12 years and itching, scaling dermatitis of both external auditory meatus for 5 years; no

previous treatment had materially helped him. Hydrocortisone ointment applied to all the affected areas gave complete symptomatic relief within 72 hours and this was followed by subsidence of erythema and scaling within 7 days. Hydrocortisone ointment was discontinued after 5 weeks of treatment and there was prompt relapse. For the next 2 months, while using the hydrocortisone ointment, symptoms were very well controlled, but again there was relapse within two or three days of stopping treatment.

Reports so far indicate that hydrocortisone ointment cannot be shown to modify immediate skin responses such as those to histamine or those of the positive scratch test. We examined from this point of view the ordinary reaction to an erythema dose of ultraviolet light. Paired exposures were made through 1.8 cm. diameter windows on the flexor aspects of the forearms of normal individuals. Two subjects received erythema doses from the Kromayer lamp, and two from a standard mercury vapour lamp. Excess of hydrocortisone ointment was applied to the area immediately after exposure, and an equal amount of ointment base was applied to the control site. These sites were protected by a plastic saucer until the ointments were removed at 2½ hours after application. All the test areas showed sharply margined bright erythema, and when reviewed at 5, 15 and 24 hours, no difference was seen between hydrocortisone-treated and control sites, in any of the 4 subjects.

In one of our patients with exudative dermatitis there was a rather poor response to coal tar on the one side and to hydrocortisone ointment on the other. When the ointments were combined and applied together the dermatitis subsided very quickly. It may be that while hydrocortisone suppresses symptoms and inflammatory signs, coal tar, where appropriate, can exert a more positive curative effect.

One of the curious things about the response to hydrocortisone applied topically is the individual variation. In some cases where relief is obtained the effect is rapid and striking; other patients with similar lesions may respond poorly or not at all. Although there is nothing to choose between the acetate and the free alcohol it seems possible that other esters may allow more effective absorption, which may be a factor in the variable response.

SUMMARY.

Clinical impressions are based on the use of hydrocortisone ointment in 71 cases of superficial inflammatory dermatoses, mostly chronic eczematous dermatitis and atopic dermatitis.

In nearly two-thirds of cases hydrocortisone had a positive effect as compared with the ointment base. Of these a quarter responded better to hydrocortisone than to any other topical therapy.

Particularly good results were seen in chronic otitis externa, in eczematous dermatitis of the eyelids and in some cases of pruritus ani.

Chronic cases usually relapsed on cessation of treatment.

Hydrocortisone ointment had no effect upon the development of erythema from ultraviolet light.

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MALIGNANT ATROPHIC PAPULOSIS : A FATAL CUTANEO-INTESTINAL SYNDROME.

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IN 1942, Degos, Delort and Tricot described a disorder characterized by papular elements with a tendency to atrophy, and by a violent intestinal episode terminated by death. We later changed our original designation of "atrophic papulo-squamous dermatitis" to "malignant atrophic papulosis" in order to emphasize this fatal prognosis, (Degos *et al.*, 1948 ; Degos, 1952). An identical observation was reported in 1948 by Tzanck, Civatte and Sidi under the name of "guttate, porcelain-like erythema" (1948). It seems that a third case was observed in France by Merklen and Cottenot in 1950. We have recently learned of two other observations, precisely comparable with these, which were described as intestinal thrombo-angiitis obliterans with skin lesions, one by Köhlmeier in 1941, the other by Lausecker in 1949, in a publication to which R. L. Sutton drew our attention. From these four or five cases, four male and one female, we may draw a clinical picture unchanging in its symptomatology and evolution.

CLINICAL FEATURES.

The skin lesions are so definite and unique that with the experience of our own case it was possible not only to identify Tzanck's case, but to foresee a fatal outcome despite the excellent general condition of the patient at the time. The cutaneous elements, scattered over the trunk and limbs, are of different ages and appear in crops. They begin as barely elevated papules, from 2 to 5 mm. in diameter, pale rose or yellowish grey in colour, and firm or oedematous in consistence. The papule soon becomes umbilicated, and the depressed centre takes on a whitish porcelain tint, with a dry, detachable scale. The margin, flat or slightly elevated, may be bright red, violaceous or pale red, and is covered with fine telangiectases. This peripheral zone is reduced in old lesions to a simple, filiform border.

As the papules enlarge they often lose their circular outline and take on irregular forms, sometimes linear or jagged, sometimes rectangular. They rarely exceed 10 mm. in size, but in Köhlmeier's case some of the "nodules" reached the size of a finger-nail, and in Tzanck's, 2 to 4 papules fused to form

a clover-leaf plaque. Although the lesions atrophy as they develop, neither complete disappearance nor true scarring has been seen.

Köhlmeier observed lesions with urticarial borders and even isolated wheals on the temple. Tzanck's patient displayed on one shoulder a large ulcerated area resembling a gumma ; it was not possible to say if this had evolved from a small papular element. Only in Lausecker's case was pruritis observed.

In all cases, palms, soles and mucous membranes were free. Lymph-node enlargement was not observed.

This cutaneous phase may last three weeks (Tzanck), seven months (Degos), one year (Köhlmeier), or three years (Lausecker), during which successive crops of papules make their appearance. The general state of health remains good. There is no fever, nor are there visceral symptoms or alterations in the blood cell picture or chemistry. Slight fatigue and loss of weight (10 kg.) was noted in our patient.

The abdominal syndrome appears with abrupt violence, accompanied by intense epigastric pain, sometimes with vomiting which may be blood-stained, sometimes with slight colicky pain. Lausecker's patient had intensely painful abdominal episodes, with signs of obstruction lasting one or two days, for a period of two years before the final crisis. Tzanck's case suffered occasional gastric upset suggesting gastric ulcer, and when the characteristic skin lesions were recognized, it was feared that he would develop in the manner we have described. His alimentary tract was therefore radiologically investigated and found normal, and a gastroscopy revealed only a small erosion of banal appearance.

In all five cases the acute abdominal syndrome ended fatally in a few days, despite immediate surgical intervention and the administration of antibiotics (Tzanck). Köhlmeier's patient survived a preliminary episode of intestinal perforation, although a laparotomy showed a small intestine perforated like a sieve with small areas of necrosis ; but he died a year later, a few days after an urgent operation for a fresh abdominal attack.

PATHOLOGY.

Histological examination of skin and gut have shown in all cases almost identical changes.

The epidermis is atrophic and hyperkeratotic. The dermis presents necrotic zones which may involve the subcutaneous tissue, and severe vascular changes are visible in the deeper layers, with thrombosis and hyaline degeneration of the vessel walls. Köhlmeier observed at the edge of the necrotic zone a vascular dilatation with irregular and partial proliferation of the intima, without modification of the adventitia. A moderate and well-defined perivascular infiltration was noted by Köhlmeier and by Lausecker.

In our case, we were struck by the absence of any inflammatory infiltration of the dermis, even around the altered vessels. The dermis was oedematous and very poor in cellular elements, with a few extravasated red blood cells and fragments of chromatin. This area forms a wedge-shaped patch extending down to the hypoderm. Köhlmeier describes the corium as invaded by avascular cicatricial tissue, with hyaline degeneration, poor in nuclei and lacking glands and hair follicles. Lausecker also notes that the skin is poor in cells and displays numerous patches of interstitial substance. Civatte, who has studied our sections, points out "the contrast between the epidermal changes and the absence of any dermal infiltrate, which confers on the sections a unique character."

The intestine exhibits zones of segmentary necrosis with vascular thrombosis. In our sections, the pathological change affected the mucosa only. This was necrotic in the whole of its depth, and the veins of the area were dilated and thrombosed. Except for an infiltration of the thrombus and the vessel lining with polynuclear cells, there was no interstitial infiltrate; the submucous and muscular coats were not invaded. Lausecker found necrosis reaching as far as the muscular layer, obliteration of arteries and veins, a vegetative endothelial proliferation of certain vessels with fibrinoid sub-endothelial substance, and a perivascular infiltrate in the areas of necrosis.

DISCUSSION.

The nosological position of this syndrome has been debated. Civatte suggests a relationship with acute lupus erythematosus, but in our opinion neither the clinical features nor the histological picture, with its absence of any dermal infiltrate, support this view. The evidence likewise gives no support to the theory of a subacute septicaemia with microbic emboli, nor to a malignant reticulosis although in this condition cases with skin lesions and intestinal perforations have been observed. In the cases under consideration, there was no sign of a reticulosis, and indeed the histological characteristic is the very absence of a cellular infiltrate.

Periarteritis nodosa has a different clinical and histological picture. In this disease, it is the tunica externa and media which are primarily attacked, and the perivascular infiltrate is much more marked.

A more difficult question is the precise relationship of this condition to thrombo-angiitis obliterans. Both Köhlmeier and Lausecker considered their cases to be cutaneous and intestinal forms of Burger's disease. Is this not an unwarranted extension of a disease which has such a characteristic picture, with its peripheral vascular location and painful necroses of the extremities, its slow evolution with successive attacks, its blood changes, and its particular terrain? The concept of a generalized affection of the vascular system, supported especi-

ally by Letzterer, has led to the assumption that in addition to the common peripheral form there may be "central forms" affecting the coronary or cerebral vessels, or an "intestinal form". This latter was identified by Köhlmeier (1940) in a case of obliteration of the superior mesenteric artery. Following this, fifteen cases have been reported in the journals, of severe or fatal abdominal crises in patients suffering from Burger's disease; in twelve of these surgical or post-mortem exploration revealed important changes in the superior mesenteric artery. But in the two cases of Köhlmeier and Lausecker which showed the clinical picture of malignant atrophic papulosis all the great vessels including the superior mesenteric artery were intact. It seems to us, therefore, risky or at least premature to classify malignant atrophic papulosis as a cutaneous and intestinal form of Burger's disease. It differs from it in the integrity of the large vessels and in its exclusive limitation to the small ones. It would be very odd if the four fully studied cases of this disease all exhibited a cutaneous syndrome which is altogether unusual, and which has never been seen in a single case of authentic Burger's disease. The intestinal lesions, moreover, are different from those observed in intestinal forms of thrombo-angiitis obliterans.

On the contrary, this association of a skin eruption of so special and easily recognizable a type, with a fatal abdominal syndrome, constitutes a clinical entity which is undeniably special both in its symptoms and its evolution. The histopathology is also most uncommon with its "uninhabited" dermal zone and meagre perivascular infiltrate as opposed to the grave vascular alterations in the deeper dermis and the intestinal mucosa.

The aetiology remains unknown. Primarily, it must surely be a thrombosing vasculitis attacking the small vessels of the skin and gut. Although our patient had a positive serology (latent syphilis) and Köhlmeier's had a dissociated serology, one can hardly suppose the condition to be syphilitic. The easy hypothesis of an allergic vasculitis rests on no supporting evidence, and the histological picture does not resemble that of the cutaneous vascular allergides so well defined by Gougerot and Duperrat, with their polynuclear, perivascular infiltrates and the fibrinoid necrosis of the vessel walls.

We must acknowledge our ignorance of the nature and nosological position of this syndrome.

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THE EVALUATION OF THE SENSITIZING INDEX OF TWO CLEANING AGENTS.

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THE object of this study was to try to evaluate the sensitizing powers of an alkaline-built synthetic detergent (A) of pH 9.8, and a 100% sodium base soap (B) of pH 10.1, both of which are in general use. There still exists controversy about the part that specific allergic sensitivity, in contrast to primary irritancy, plays in the production of dermatitis due to these products.

The big problem is to try to anticipate potential sensitizing agents in the many new products marketed to-day before trouble arises from their widespread use. No really satisfactory method yet exists, whether by patch tests or immersion tests, and the final test is one of actual usage, when a large section of the population is exposed to these substances for several years.

Schwartz and Peck (1935) have recommended a prophetic patch-test procedure in which a group of 200 persons or more have the substance applied in 48-hour patch tests, and then the same group are re-tested in 14-21 days ; those whose patch tests have changed from negative to positive are deemed to have become sensitized. The disadvantages of this method seem to be that the substance would have to be a highly potent sensitizer to give significant results, and that large groups are required.

Jadassohn (1923) stressed the importance of repeated applications of antigen to produce sensitization in human beings with simple chemicals. Brunner *et al.* (1952) developed a technique in which the test material was applied to the skin in the concentration in which it is used, for a period of time similar to the normal period of contact. Applications were repeated daily for 5 days, a different area of the forearm being used each day to eliminate possible summation of primary irritation effects. After an interval of 7 days, reapplication was commenced, and continued until reactions developed, or until the end of the test period ; the second series was intended to reveal sensitization and to allow for repetition of contact so as to obtain high yields. Positive reactions consisted in the development of eczematous lesions lasting over 24 hours at the test site, and in some the simultaneous flare-up of distant previously tested sites. Concurrently patch tests which were originally negative in all cases were now shown to be positive. Three mercaptans to be used in hair-waving

agents were tested in this way on a small group of persons ; one was found to be a definite sensitizer, another an irritant, and the third only a poor sensitizer.

In my own study, several modifications were made to suit the particular circumstances. 50 normal healthy male volunteers taking part were kept under strict daily observation throughout a 3-week period in March to April, 1953. Their backs were divided off into four quadrants—two small upper and two larger lower. The former were reserved for the routine 48-hour patch tests to be done both before and after the applications, and the latter for the daily application of detergent (A) on the left and soap (B) on the right. The men were divided into four groups—Groups 1 and 2 consisting of 20 men each, Groups 3 and 4 consisting of 5 men each.

Group 1 had warm 1% solutions of (A) and (B) at 40° C. applied to the left and right lower quadrants of their backs respectively on large 4 in. $\times$ 4 in. four-ply gauze pads, covered by plain cellophane, for 2 hours daily for 5 days at different sites ; an interval of 10 days was allowed to incubate sensitivity, and then 15 consecutive daily applications were again applied, or until such time that a reaction occurred.

Group 2 similarly to Group 1, except that 10% solutions were used.

Group 3 had 1% solutions applied, but to the identically same area each day for 15 consecutive days.

Group 4 similarly to Group 3, except that 10% solutions were used.

Throughout the period of applications reactions lasting up to 24 hours occurred only in Group 4. They involved all 5 men when using 10% solutions on identically the same area, where there was a summation of primary irritation effects—on the 7th and 10th days with (A) and on the 9th, 10th and 13th days with (B). There were no persisting eczematous reactions in any of the four groups.

All 50 men were tested with 48-hour standard patches both before and after the daily applications, using serial concentrations of (A) and (B) of 1%, 2.5%, 5% and 10%. The results are shown in Table I.

TABLE I.—*Results of Patch Tests before and after Daily Applications.*

	(A).				Total.	(B).				Total.
	1%.	2.5%.	5%.	10%.		1%.	2.5%.	5%.	10%.	
Before :										
No. of reactors	0	0	1	2	3	0	2	12	18	32
After :										
No. of reactors	0	0	3	6	9	0	0	4	9	13

It can be seen at once that none became sensitized ; there were no persistent eczematous reactions to the daily applications, nor were there any flare-ups of previously tested sites, and patch tests remained negative in the concentrations of 1% and 2.5% at the end of the experiment.

From the patch test results in Table I, two interesting facts are confirmed, however: (i) That pure soap (32 reactions) appears to be more irritating to the skin under a closed patch test than the detergent (A) (3 reactions); (ii) that the total number of reactions on the same group of men at the end were less (22) than at the beginning (35); 13 who had reacted initially failed to do so on repetition.

One might argue that if these were primary irritants, their reactions should be consistently repeatable; but I would like to emphasize from personal experience of performing over 3000 patch tests with a variety of soaps and synthetic detergents on normal subjects, that considerable irregularity and variation of response is one of their characteristic features.

Statistically, according to Henderson and Riley (1945), if the reaction rate in the general population is 1:1000, in any random group of 200 subjects, at best 82% will be non-reactors. Likewise, even though no reactions are observed in a sample group of 200, it is still possible to have a reaction rate as high as 1.5% in the general population. I surmise that under my own experimental conditions, where very large areas of skin were exposed to both the alkaline built detergent (A) and soap (B), they must both be extremely poor sensitizers; they act, rather, as mild primary irritants. In hand laundry washing, the ordinary housewife uses detergents in about the percentage of 0.3% but the concentration in the lather usually runs about 8% varying from about 5 to 20% (Morris, 1953). It is reasonable to suppose that there can be a build-up in concentration, particularly in the interdigital clefts and under rings, if the hands are not properly rinsed but merely dried, as is quite frequently the case in patients whom I have questioned.

A much more important and interesting approach is the investigation into the possible ways in which soaps and detergents might damage the skin by their direct chemical action. Szakáll (1941) showed that the non-alkaline synthetic detergents Praecutan, pH 5.4, and Satina, pH 7.4, degreased the skin more than soap, while Neuhaus (1951) demonstrated that both soaps and synthetic detergents degrease the skin initially to much the same degree after immersion for half an hour in 1% solutions at 40° C., but that the lipoid regeneration capacity of the skin is much more disturbed by synthetic detergents than by soaps. In addition to this effect, their alkalinity must be taken into account, for many of them contain in the region of 50% alkaline builders, so that the rate at which the skin neutralizes alkali may also play a rôle, as shown by Burekhardt (1947).

Schneider (1953) believed that apart from physico-chemical phenomena due to their wetting and penetrating properties, a chemical reaction occurs with the formation of protein salts, leading to a fundamental denaturing of the epithelium. Kuchinka (1950) also stressed the affinity of synthetic detergents for keratin. Earlier Anson (1941) demonstrated that under the influence of

sodium lauryl sulphate (one of the Duponols) the enclosed sulphydryl groups of native egg albumin were exposed and became titratable, but that prior to the action of the detergent these groups do not react with sulphydryl reagents. Jones (1943) demonstrated the dispersing effects of Duponol on various keratins, which supported the evidence that denaturing occurs with these proteins as well.

Since no quantitative data were available on the denaturing effect of soaps and detergents on skin proteins, Van Scott and Lyon (1953) determined whether a 1% solution of a variety of these products altered the keratin molecule in such a way as to expose sulphydryl groups from various types of human keratin. After incubation with these solutions for one hour at 40° C., the measurable amounts of sulphydryl groups were increased over those of control solutions. These findings indicate a certain denaturing effect of these substances on the keratin molecule. It seems highly probable that, among several other factors, this alteration of the molecular structure of keratin as demonstrated by our values is an important but not the only mechanism in the production of dermatitis by detergents as a group. It may well be that there is a synergistic action of these organic wetting agents and their alkaline builders, though so far as the latter are concerned I am impressed with the remarkable buffering capacity of keratin and feel that the pH factor has been over-stressed in the past.

SUMMARY.

Both the alkaline detergent and soap are poor sensitizers, but act as mild primary irritants.

Patch tests with these substances show a wide range of variability even when repeated on the same volunteers within a short space of time.

More recent research has concentrated more on the denaturing effect of the synthetic detergents on keratin.

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CUTANEOUS PORPHYRIA IN THE ADULT.

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SINCE 1951 we have been able to make quite a thorough study of seventeen cases of a bullous affection of the skin which fits in with the porphyria group.

It is entirely different from the acute abdominal and nervous type of porphyria, and it appears also to differ from congenital porphyria or Gunther's disease. We shall discuss its relationship to the late type of cutaneous porphyria of Waldenström, known also as chronic porphyria of Gunther. Cases similar to our own had previously been described in 1944 by Szodoray and Sumegi under the name of chronic cutaneous porphyria, in 1947 by Brunsting, Mason and Aldrich, and in 1950 by Borda and Campins who classified them under the name of bullous and erosive porphyria of the adult. Recently, Barnes and Marshall have reported similar cases among the Bantus in South Africa. However, none of these authors appear to have carried out histological examination of the skin lesions or a complete chemical study of the disease.

The clinical examination of our patients has in each case been completed by a consideration of the histology and by accurate chemical studies, and the data which we have been able to produce in these three fields enables us to regard the adult form of cutaneous porphyria as a special nosological entity and to distinguish it clearly from other bullous affections.

Cutaneous porphyria is seen from the commencement of adult life and sometimes occurs even in old age. The age of our patients at the onset of their illness was between 39 and 66 with a marked predominance in the male (15 males and 2 females).

Clinically, the affection is characterized by a dermatological syndrome which is nearly always associated with the passage of urine of a peculiar reddish-pink colour, at least during the development of the attack. The dermatological syndrome is in itself quite characteristic: The essential lesions are bullae which appear in groups of 6 to 12 on healthy skin. Sometimes they are surrounded by a narrow erythematous zone, and they are usually associated with pruritus or a feeling of tension. Vesicles also occur; they are globular and contain clear serous or even blood-stained fluid. They vary in size from that of a pin's head to 2 or 3 cm. in diameter. The evolution of the lesions is rapid; they may appear as a pink oozing macule or become dry soon after they have formed and present as a rounded dried-up crust which soon falls off. Whatever the mode of development, a pink, slightly pigmented macule

or a round depigmented patch is left. Eventually the lesions disappear completely. Secondary infection may occur, but it is not usually serious.

It is important to emphasize the distribution of bullae, which appear only on exposed parts and generally attack first the dorsal and outer aspects of the fingers, often in the neighbourhood of joints, the thumb, index and little finger, and extensor and outer aspect of the wrists. The palms are rarely involved, and even more rarely, the forearms and elbows if these are commonly exposed. Finally, bullae appear on the head and neck, especially on the glabella, ears, forehead, pre-auricular region, temples and also the nape and sides of the neck. The bullae have a tendency to pick out areas where the skin directly overlies bone or cartilage without any intervening muscle. It is exceptional for the lower extremities to be involved, except when they happen to be unprotected by clothes. With the bullae there appear, in due course, atrophic macules, milia, and pigmentation.

The atrophic macules consist of round or oval patches, whitish or pink in colour or even slightly pigmented. They are several millimeters in diameter and have a predilection for the extensor aspects of the fingers, especially in the neighbourhood of the metacarpo-phalangeal joints, but they are also seen on the nape of the neck and the face. By becoming confluent they may give rise to an appearance which resembles scleroderma. They appear secondarily either in the scarring of a bulla or as the result of some trivial injury, thus demonstrating the extraordinary fragility of the skin of these patients. They disappear eventually.

Milia are very frequent. They consist of fine whitish granules about the size of a pin's head, having a similar distribution to the bullae with a predilection for the extensor aspect of the fingers and the cheeks where they are often associated with comedones. They disappear spontaneously and leave no trace.

Pigmentation is likewise constant but varies considerably in its appearance. It is of a grey or brown colour and tends to be disposed in a reticulate pattern or in patches. When it is diffuse it is reminiscent of chloasma, Riehl's melanosis, or even of vitiligo. It is remarkable for the way in which it picks out the temporo-malar regions. It may also extend to the retro-auricular regions, nostrils, peri-oral regions, the neck or even the forearms. It is only exceptionally generalized. It may be seen along with ephelides on the shoulders and arms.

The appendages are practically unaffected. The nails are normal; the hair, generally brownish in colour, is usually thick (especially the eyebrows) and a certain degree of hypertrichosis is present, especially in women; a seborrhoeic type of baldness is not uncommon. The reddening of the teeth, a constant sign in congenital porphyria, is absent in these cases. The mucous membranes are also normal.

With this dermatological syndrome is associated, especially during the earlier stage of the attack, a peculiar discoloration of the urine which demands close study because in about 50% of the cases it passes unnoticed by the patients themselves. Sometimes, on being passed, the urine is reddish-orange, or frankly pink in colour; at other times it is almost normal and it may be necessary to collect it in a glass and to examine it with the light falling obliquely in order to detect the typical pink tinge in the meniscus. Quite often the urine darkens after exposure to the air for several hours. We would like to emphasize the point that this colour varies in intensity at different periods and even at different times of the day in the same patient. Sometimes it is predominant in morning specimens and sometimes in evening ones, and it may disappear altogether during periods of remission.

Certain associated affections such as duodenal ulceration, psoriasis and diabetes do not appear to us to be anything more than coincidences.

Examination of the other systems is generally negative with the exception of hepatomegaly without subjective signs and without any constant alteration in liver function tests. A history of chronic alcoholism is quite usual.

Cutaneous porphyria of the adult occurs in attacks which always commence in the spring or early summer, which manifest themselves by a bullous eruption involving the upper extremities, and during the course of which the presence of crusted lesions, atrophic macules, bullae in all stages of development, and milia all make up a very characteristic clinical picture. As the disease progresses the bullae become rarer, and in the course of a few months they disappear altogether. Eventually, during the course of a fresh attack the lesions spread not only to the upper extremities, but also to the face and neck. However, the incidence of the disease is seasonal in only certain people, and the bullae can occur in autumn or winter; sunlight plays an important, but not an essential role in the recurrences, and the disease may develop quite apart from exposure to sunlight. We have never elicited Nikolski's sign, but these patients are peculiarly sensitive to the slightest trauma, which gives rise either to ordinary injuries or to blisters.

In some cases the disease appears to become chronic (in two of our patients it had already been present for 7 to 8 years at the time of examination), but it is interesting to note that it may regress slowly over many years (8 to 15 years). Even in these chronic cases, the general health remains satisfactory. The disease, although painful, does not appear to be serious and we have never lost a single patient. Such a benign condition differs greatly from acute porphyria which is fatal in 60% of the cases, and from congenital porphyria in which the prognosis is always guarded.

Histologically, cutaneous porphyria appears quite characteristic. Our biopsies, which have all been carried out on bullae from the palms and fingers, have revealed changes so similar that it is possible to pick out a number of

common features. The roof of the bulla is formed by the whole thickness of the epidermis, and it is thrown into folds and always covered with a thick horny layer. The floor of the bullae presents a peculiar fringed appearance, bristling with "villi" which are usually elongated, but at times digitate or filiform. These "villi" contain dilated capillaries but there is no inflammatory reaction to be seen here or in the dermis. Finally, the bulla is almost empty, except for a little serous fluid, and cellular elements are absent or consist only of occasional polymorphs or mononuclears. The elastic tissue of the corium is often thin. Having regard to the structure of the bulla it is obvious that cytological examination of the fluid is of no value.

To sum up—the histological picture conjures up that of Duhring-Brocq's disease to which it has been likened by certain foreign authors, but from which we believe it can be distinguished by the fringed appearance of the floor of the bulla and by the emptiness of its lumen. These features are especially clear in fresh bullae, and disappear when secondary infection supervenes.

The milia consist of more or less rounded cavities bounded by a rather thin Malpighian layer which is cast off or destroyed after an inflammatory reaction produced by foreign body cells.

All our patients were submitted to detailed chemical investigations by one of us (J. C.), but the description of these tests will not be dealt with here (Bolgert, M., Canivet, J., and Le Sourd, M. 1953).

The essential fact is the detection in the urine of these cases, by the method of Rimington and his collaborators, of considerable quantities (but with daily variations) of uroporphyrin (8-carboxyl porphyrin) at the rate of 3.5 to 14 mg. daily. It must be remembered that normal urine contains no uroporphyrin and only minute amounts of coproporphyrin.

By various methods such as chromatography, spectrophotometry, fractional crystallization and a study of the melting point, we have been able to establish that it consists of a mixture of uroporphyrin I and uroporphyrin III with a predominance of one or the other, according to the case. Besides this, we have found traces of other porphyrins (4-, 5-, 6-, 7-carboxyls). These findings are of fundamental importance, since they enable us to distinguish cutaneous porphyria of the adult from congenital porphyria in which the urine contains uroporphyrin I, and from acute porphyria, in which uroporphyrin III predominates. We wish to make it clear, however, that in spite of their importance, such complicated investigations are not essential to confirm the diagnosis in every-day practice. Besides the pinkish colour of the urine, the red fluorescence in ultra-violet light, and the presence of an absorption spectrum with two bands (580 and 540 $m\mu$) in the green, or more rarely four bands (500, 540, 580 and 620 $m\mu$) provide sufficient evidence to establish the presence of a considerable amount of porphyrinuria. We may add that the method of Watson and Schwartz which is intended to demonstrate

porphobilinogen in the urine has always given negative results in our hands. Finally, attention should be drawn to the tendency among several patients to a raised blood iron.

Thus cutaneous porphyria of the adult is quite typical clinically, histologically and chemically and its diagnosis is straightforward. The incidence of the affection is not negligible since we have found 17 cases in 3 years, and it is certain that it has often been confused with other bullous conditions, which we shall mention briefly :

Dühring's disease even in its atypical forms, is not confined to the exposed parts, and the bullae, likewise subepidermal, contain many cells especially eosinophils. The floor of the lesion, which is always more or less inflammatory, never presents such a regularly fringed appearance ; it may also be rectilinear, wavy or irregular in form. Erythema multiforme bullosum has the same localization and also occurs in attacks, but the bullae are always associated with the characteristic maculo-papules.

In view of the indisputable, if not determining, role played by sunlight in cutaneous porphyria, its relationship to the light sensitizations is worthy of discussion. Dermatitis pratensis (Oppenheimer) has a different appearance and could hardly be confused with it, nor could certain " light sensitizations " brought about by drugs. Moreover, the histology of these cases is more like that of erythema multiforme bullosum, and uroporphyrinuria is absent. Only the very rare epidermolysis bullosa simplex appearing in early childhood has a similar histology, but here, uroporphyrinuria is absent. As to epidermolysis bullosa dystrophica, it seems certain that a proportion of these cases should be regarded as cutaneous porphyria.

It only remains to consider the classification of this dermatosis within the general order of the porphyrias. Its clinical aspect, its mode of development and its biochemical features all serve to differentiate it from the acute abdominal and nervous type of porphyria. Moreover, its onset in adult life or old age, the absence of involvement of the appendages (except a slight hirsuties) and of other trophic disturbances, its development in attacks, and the chemical findings in the urine would hardly admit of its being regarded as a late form of congenital porphyria.

Is our type of porphyria comparable with the late type described by Waldenström and Gunther ? This occurs in the young adult and is characterized clinically by the alternate appearance of a bullous eruption and abdominal symptoms. Moreover it is frequently fatal in its subacute forms. The cases described by the English authors (Thompson, MacGregor, Wells, Troit) and studied chemically by Rimington and others, appear to belong to this variety. The porphyrins isolated in these patients are sometimes uroporphyrin I or III and sometimes coproporphyrin I or III with the possible presence of porphobilinogen at an advanced stage. In our patients, we have never observed

any abdominal symptoms or an acute onset. Until fuller information is available, we shall continue to believe that cutaneous porphyria is a distinct nosological entity.

In our ignorance of the pathogenesis of the porphyrias, whatever the variety, the treatment can only be symptomatic. Protection against direct sunlight should be advised, and the wearing of broad brimmed hats encouraged. The hands should be protected by gloves, and creams containing screening agents should be applied to the skin of the exposed parts. Vitamin PP and liver therapy are ineffective. The action of vitamin B12 and B2 is likewise very debatable.

However, disappointment at our present state of therapeutic ineffectiveness may be softened when it is realized that this is but a relatively benign affection—a fact which has not yet been denied.

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LETTER FROM GERMANY.

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and

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ANY attempt to give a résumé of all German dermatological research, say since 1948, in the form of a letter must fail; there are too many papers for the limited space. Besides, many German dermatologists had the good fortune to produce their results at the outstanding 10th International Congress in London.

In September, 1953, the German Dermatological Society met in Frankfurt, and practically all fields of dermatology were considered. The seven main subjects and the speakers were: physiological and pathological functions of the skin—Ebbecke (Bonn), Rothman (Chicago), and F. Herrmann (New York); actinic dermatoses and light protection—Kimmig (Hamburg); progress in dermatological radiotherapy—Wachsmann (Erlangen), Proppe (Kiel); X-ray therapy as an integral part of dermatological therapy—Schreus (Düsseldorf); pemphigus and pemphigoid dermatoses—Touraine (Paris); clinical features and therapy of melanoma—Miescher (Zürich); and clinical features and therapy of congenital syphilis—Arzt (Vienna). The names of the speakers show the close association between German dermatologists, German-speaking of other countries, and other European and North American dermatologists. In what follows, therefore, a few papers of foreign German-speaking authors will be mentioned.

A congress is a landmark in the life of a specialty and of science. We propose, therefore, to take the Congress of the German Dermatological Society as the starting point of our review and to consider only developments which have taken place since. With the existence here of so many research institutes in universities and hospitals we cannot stress their individual direction of work; there is no centralization and the many sidedness of the clinics is very great—sometimes, considering their limited means, too great.

The problem whether morphology reveals aetiology crops up repeatedly in clinical description and histology. In a review, actually planned for the London

Congress, Gans (1953) discussing connective tissue changes, denies, like Klemperer, the validity of considering the collagenoses as of a common aetiology. In the literature of the last few years cases of Melkersson-Rosenthal syndrome have been repeatedly described. Hering and Scheid (1954) report two further cases and regard this disease picture, as others do, as a form of sarcoidosis. Schuermann (1952) and Braun-Falco and Rathens (1953) found eruptions closely related to cheilitis granulomatosa occurring also on the head; Schuermann mentions parotitis, and glossitis granulomatosa. Neither the histological tuberculoid structure nor the presence of other features suggestive of sarcoidosis can, however, be taken as proof of aetiology.

Further investigation of dermatoses calls for their sharp morphological differentiation. It is to be welcomed, therefore, that Stühmer (1953) distinguishes onycholysis semilunaris purulenta from the group of diseases featuring loosening of the nail. It begins with invasion of pyogenic organisms under the nail plate, and later the nail is raised in half-moon fashion. In this connection it may be mentioned that Reich (1952) found (for the first time) the causative organism of toxoplasmosis in nodular swellings which histologically resembled those of spotted fever. Another new observation is a case of Hoffmann (1953) of a "woolly hair naevus" (naevus ulotrichicus capillitii unilaterialis) which he had followed since 1917. Woolly hair appeared in a circumscribed area of otherwise sleek hair.

The number of diseases where phlebitides of the type of phlebitis migrans occur with a concomitant endarteritis obliterans is increasing (Elschner, 1953). Phlebitis "fil de fer" (Favre), so far observed only in France, has now been recorded in Germany with a case of so-called Mondor's disease (Braun-Falco, 1953).

Hauser (1953) has investigated the presence of tissue mast cells in bone marrow and lymph nodes. It was shown that certain diseases apparently restricted to the skin, such as acrodermatitis atrophicans (Herxheimer), are in reality generalised disturbances.

Wulf (1954) has confirmed the investigations of Kimmig in an extensive work on the light dermatoses. In patients with polymorphic light eruptions the latter found, spectroscopically, a light band at 500μ , and Wulf has now pointed out the photodynamic action of the substances which were producing this band. Langhof and Sprössig (1954) regard light sensitisation as a photo-oxidation which can be inhibited by strong reducing agents, such as BAL. Porphyrins in the skin of the face can frequently be demonstrated by the use of Wood's light.

Klärner and Krückemeyer (1954) rightly doubt the necessity of demarcating as a special entity the so-called "pigmented lymphogranuloma with skin changes." The lipomelanotic reticulosis of Pautrier and Woringer is, with increasing observation, regarded more and more as a nonspecific accompani-

ment of itching dermatoses. In the course of one year Elschner and Lennert collected 19 such cases in our clinic. The disease has no connection with Brill-Symmers disease, although it is often confused with it.

The statistical evaluation of the course of dermatoses is often of great significance, for single observations from which conclusions cannot be drawn acquire significance when multiplied. For example, Böhmer and Heite (1953) showed in this way that in mycosis fungoides, the *tumeurs d'emblée* varieties correspond prognostically to the tumour stage of the more usual case. This does not necessarily signify that these varieties are a disease picture belonging to mycosis fungoides, but only that mycosis fungoides, once it becomes a connective tissue tumour, takes on the course of the latter.

Previous investigations on the inheritance of neurodermatitis diffusa are added to by a case of Höcker (1953) who observed concordant appearance in uniovular twins. Jung (1953) reports on a case of so-called granuloma faciale localized other than on the face. According to the clinical description and histology it appears to be a lymphocytoma with many eosinophils.

Greither and Tritsch (1953) report on lichen Vidal urticatus, a disease picture originally described by Schönfeld. Seen more often in preseniles or seniles, it is variously classified: papules found on the extensor surfaces of the extremities are reminiscent of lichen Vidal, but they never join up to form plaques.

On the evidence afforded by 10 cases of his own, Steigleder (1953) regards the haemorrhagic pigmentary dermatoses (Majocchi, Schamberg, Gougerot-Blum) as closely connected syndromes. Clinical and histological differences do not suffice to make a distinction, a view in accord with Montgomery and his colleagues. Pfleger (1954) sees in these diseases disturbances of the "end-stream current". We have, thereby, reached the *Relationspathologie* of the pathologist Ricker, which was introduced into dermatology by Gottron, and which is used by him and his pupils to explain the most variegated disease pictures, especially the so-called metabolic diseases. Woeber (1953) also deals with Ricker's concepts. It is not remarkable that such a strong emphasis on vessel changes, e.g. on capillary dilation in the histological picture, invites criticism. One must agree with Stühmer (1953) who reminds us of the wide difference which exists between the microscopical picture and conditions in the living subject—a gulf which cannot as yet be bridged; capillary dilatation can even occur after the removal of the tissue from the organism. The experiments of Illig (1954) also raise doubts on the correctness of Ricker's assumptions. The investigations of Röckl, Metzger and Spier (1954) concerning exudation of serum from vessels, determining protein content electrophoretically, allow one to assume a decidedly more complex state of affairs than can be expected from the *Relationspathologie*. Certain it is that behaviour of vessels, though important, is only one factor. These doubts concerning the reality of histological structure must, however, not be driven too far. In psoriasis

and neurodermatitis, for example, the state of the capillaries observed in the living subject corresponds to that of the histological preparation.

In the field of histology, the findings of Schreus *et al.* (1953) and of Schreus and Schulten (1953) are very stimulating. Not only could they confirm that the epithelium of the buccal mucosa changes during the menstrual cycle but they could also demonstrate a corresponding behaviour of the epidermal cells cytologically. Sebum production was shown to be increased in the second half of the menstrual cycle and to fall away again postmenstrually.

Following on the well known results of the anatomist Stöhr, and the pathologist Feyrter, mention must be made of investigations on the terminal reticulum of the vegetative nervous system and its organs. Changes occurring in dermatoses have been recorded by John, by Ormea, Wiedmann, and by Nödl (1953). Recently Knoche (1954) of the anatomy institute of Münster and Bonn reported changes in the vegetative nervous system in the skin of the bald scalp. Thies and Glogengiesser (1953) found hyperplastic nerve substance and degenerative changes in the terminal reticulum of glomus tumours. These investigations are in a field neglected in dermatology. So far nervous structures, above all the elements of the autonomic nervous system, have not received much attention with the notable exception of some authors, such as Pautrier. These findings, although they augment our present concepts, must be received with reserve and do not permit generalizations. The technique is difficult and for this reason only a few cases have been investigated. Judgment will depend upon the further elaboration of one experienced in this field, but the results so far obtained should encourage those who undertook this praiseworthy work.

Weyhbrecht and Korting (1954) again worked out Lundt's case of hyalinosi cutis et mucosae and it appears that one may be dealing in this case, as in the whole disease picture, with a special form of amyloidosis (para-amyloidosis?).

Nödl (1954) gives a thorough dissertation on transitional cell epithelioma. He regards this lesion, well known to histologists, as a mutation of basal cell epithelioma, which naturally could be a malignant one. In the further development of the tumour, the soil is the deciding factor. Endometriosis of the skin, so far totally neglected in dermatology, is important in the differential diagnosis of skin tumours. Kliegel and Krinitz (1953) give an excellent review following on a case of their own.

Braun and Hieronymi (1954) have shown in animal experiments that parenteral chlorinated naphthalenes produce liver, renal and pancreatic damage. Numerous cases of chloracne arose here as in other European countries immediately after the war, and until lately exanthematic outbreaks simulating an infection (cable rash) could be observed. Landes and Herger, of our clinic, produced changes in rabbit skin and liver by external inunction of chlorinated paraffins. These investigations will later be published in detail.

Tronnier and Wagener (1953) report on the entry of ointment bases containing

radioactive substances into the skin. In confirmation of previous findings eucerin and adeps suillus were absorbed four times as rapidly as vaseline; the final concentration within the epithelium is the same with all three substances. Kleine-Natrop and Gerauer (1953) found that cod-liver oil ointment and zinc oxide cooling ointments contained more unsaturated fatty acids than vitamin F preparations obtainable commercially, but not than the oily concentrates.

Von Glasenapp and Leonhardi (1953) dealt with fermentative processes in the skin. Oxydative mechanisms, as shown by determination of glycolysis, citric acid cycle and the cytochrome oxydase-cytochrome system took place as in other organs. Braun-Falco's (1953) histochemical investigations on glycogen content in acanthosis confirmed previous results of Steigleder (1953, 1954).

Therapy is a field in which the constant desire to use the most modern methods results in the old and well tried being neglected and therefore not mastered. The work of Schmidt-La Baume and Lietz (1953) should be mentioned as an appraisal of ointments, powders and other external remedies, which appear to us to be sometimes regrettably neglected by the newer foreign authors. We can refer only briefly to the thorough discussion on the therapy of skin tuberculosis, relatively common in Germany, in the paper of Marchionini (1953), with stimulating studies on ethnology and dermatology, to Schreus (1953) and to Meyer-Rohn and Schulz (1954).

In conclusion a new therapy should be mentioned. The Hoechst dye-works have produced an arsenic-free non-metallic antisyphilitic substance from the group of the 1, 3 substituted triazenes, since it was found that the newly developed spirotrypan, an improved salvarsan, offered no decided clinical advantages over neosalvarsan. The same firm have brought into commercial use an arsenious oxide under the name Haemosept, which can kill the spirochaete of relapsing fever and syphilis present in blood for transfusion in such small concentrations as to have no toxic action. At the Paul Ehrlich-von Behring Celebration which took place on the centenary of their birth on 14 and 15 March 1954 in Frankfurt and Marburg, Kimmig reported on a new antisyphilitic called Melusin. The first clinical results are favourable, but a definite judgement must be reserved on account of the short period of observation and the present lack of cases of syphilis.

Finally, two books from the German literature may be mentioned. The first is that of Carrié (1951) on occupational dermatoses. He presents a concise and clear review appropriate for the practising dermatologist. The book by Siemens (1952) on general diagnosis and therapy of skin diseases would be suitable to give dermatologists all over the world an understanding of their nomenclature on account of its extraordinarily clear expositions and its really excellent illustrations.

While we join in this letter the grateful memories of the London Congress of 1952 with the best wishes of German dermatologists for our British colleagues

we hope that later reports from Germany—this beginning apart—will give a wider, more complete and far-reaching review.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. R. T. BRAIN.

19 November 1953.

Lymphoma of Mycosis Fungoides Type Treated with Mepacrine (Three Cases).—Dr. C. H. WHITTLE and Dr. J. L. MOFFATT.

I.—R. J. H—, a bricklayer aged 59.

History for $6\frac{1}{2}$ years of scaly, red, psoriasiform, figurate, mildly itchy eruption on trunk and limbs which healed in places and spread in others. Some mouth lesions present.

First seen 22 February 1952. Large circinate areas on trunk and legs, with infiltration of some of the bluish-red plaques arising on the site of old lesions. Pigmentation but no atrophy is left after healing. No enlargement of spleen or lymph glands.

Wassermann and Kahn negative. Blood count normal.

Histological section showed a fairly typical picture. The cells comprising the very dense infiltrate in the corium are pleomorphic and show some 'mycotic cells.' Pautrier micro-abscesses are present.

Course.—Cortisone ointment produced no effect. Thorium X varnish slight temporary effect. U.V.R. also had temporary effect.

11 September 1953: More infiltration, especially of thigh lesions. Mepacrine 0.1 g. orally twice daily started. After 2 months most of the lesions have shown varying degrees of fading, leaving some pale-staining areas. There are still infiltrated areas projecting 1-2 mm. above the surface.

II.—G. W—, a lorry driver aged 40.

History of widespread figurate, scaly, psoriasiform erythema on trunk and limbs, healing and relapsing for 13 years. In 1944 infiltration of some of the lesions and considerable enlargement of lymph glands in groins and axillae were noticed.

1946: Biopsy confirmed the diagnosis.

1948: Differential blood count normal. Improvement followed course of U.V.R. Thorium X painting ineffectual.

1951: Lymph glands larger and firmer. Liver and spleen palpably enlarged and have remained so most of the time.

21 January 1953: Full blood count normal.

21 September 1953: Biopsy from infiltrated lesion on right thigh. "Moderate acanthosis with parakeratosis, moderate cellular infiltration of papillary layer: cells variable, mainly lymphocytes and histiocytes. In places the infiltration extends into the epidermis, especially over the tips of the papillae. The picture is consistent with mycosis fungoides."

Present condition.—Red scaly plaques over face, limbs and trunk, with confluent areas over buttocks and thighs. Raised infiltrated lesions on wrists and forearms.

Tumours.—One 1 in. diameter in groin and another under left arm. The right

frontal area of scalp shows a patch of hair loss with redness and scaling. Latterly the lesions are less responsive to U.V.R. Mucosae not affected. Itching prominent.

Mepacrine 0.1 g. twice daily orally started on 11 November 1953.

III.—E. H.—, a married woman aged 61.

History of 15 months' eruption on trunk and thighs of bluish-red circular plaques with some infiltration and scaling, only moderately itchy. There was a tumour 4 in. diameter on right thigh projecting $\frac{3}{4}$ in. above surface. History of gastric ulcer 7 years ago. General health fair. Family history *nil ad rem*.

First seen 20 May 1953. Blood count normal except monocytes 14%, or 1176 per cmm. and slight hypochromia. Wassermann and Kahn negative.

Biopsy 3 June 1953: Typical mycosis fungoides. Later biopsy: "The clear cellular exudate is still pleomorphic, but the cells are becoming more uniform and primitive. Some doubtful mycosis cells."

Course.—She was put on to mepacrine 0.1 g. daily, and the lesions after four or five weeks became paler and flatter and some which had broken down healed. Mepacrine was discontinued because of congestive heart failure and the lesions became more active again. Admitted to hospital 26 September 1953. Liver enlarged $1\frac{1}{2}$ inches down and spleen 2 inches. Cervical lymph glands enlarged, firm and tender; inguinal glands moderately enlarged. There was continuous mild pyrexia. Mepacrine 0.1 g. given daily for 17 days, then 0.1 twice daily for 14 days, then once daily for 8 days, then stopped. The skin became tinged yellow in a week or so and the lesions began to regress after two or three weeks. She developed purpura in the lesions and on 11 November 1953 an infarct in the spleen. The purpura was associated with a low platelet count 56,000 per c.mm. and a strongly positive capillary fragility (Hess) test. Ascorbic acid 0.32 mg. per 100 ml. The platelet count returned to normal on 12 November 1953.

On 3 November 1953 "blast" cells appeared in blood count for first time, 14%, or 1680 per c.mm., and increased 9 days later to 36.5%, or 3212 per c.mm. Anaemia accompanied this change. R.B.C. 2.97 million per c.mm. and haemoglobin 8.0 g. per 100 ml. Marrow count shows 80% "blast" cells. The skin is tinted yellow. The redness and infiltration of practically all the lesions have disappeared leaving brown pigmented discs with deep yellow staining in some. The lesion on the right thigh has diminished in all its dimensions. Her general condition is poor and the picture is changing towards a lymphoblastic leukaemia. Such a change is not unknown nor very unusual. Keim, Warthen and Wile (quoted by Forkner) regard mycosis fungoides, lymphoid leukaemia and Hodgkin's disease as forms of lymphoblastoma and there is wide support for this view: e.g., Ormsby and Montgomery include mycosis fungoides, various types of leukaemia cutis, Hodgkin's disease and lymphosarcoma of the skin under the term lymphoblastoma, and remark that mycosis fungoides may terminate as one of the other lymphoblastomas. Alternatively one could regard this case as a lymphoblastic leukaemia from the start, though the histology does not altogether support this view. The mepacrine had no apparent effect on the blood picture or ultimate course.

(*Note*.—This patient died the day before the meeting—probably from heart failure.)

Comments.—Three cases of lymphoma of mycosis fungoides type have appeared to respond to acridine compounds. In the first case (not shown to-day) euflavine (Muller, 1937) was given intravenously—6 daily doses of 25 c.c. of a 2% solution—and resolution of the skin lesions started in 3 days. In the other two cases a few weeks on mepacrine by mouth elapsed before any response was noticed. The response appears to be associated with skin pigmentation from the drug: cf. Page (1951) on treatment of lupus erythematosus. In the first case there has been a remission for 7 years.

The chemical formulae of euflavine and mepacrine have a common acridine base.

Spontaneous remissions in mycosis fungoides are the rule, some apparently permanent. We can only claim that these compounds appear to induce a remission rapidly where the usual remedial measures have failed. They are less toxic than nitrogen mustard, or P₃₂, and one of them, mepacrine, can be given orally.

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Secondary Carcinoma of the Skin.—Dr. W. G. TILLMAN.

I saw this patient first on 8 October 1953 with a lesion that first developed in March 1953. When noticed it was the size of a pea, but has now gradually increased to about 3 in. in diameter. The reddish yellow lesion reminded me of a reticulosis and was situated on her right arm, extended deeply and was very hard to the touch. On making a biopsy the sensation was that of cutting through a carcinoma.

Dr. Whimster reported: "Secondary carcinoma. The cells are small, round or oval and have no apparent cytoplasm. The appearances suggest that the primary might be in the lung."

W.R. and P.P.R. were negative, and the blood count was normal.

Physical examination showed no lesion elsewhere and skiagram of the chest was normal.

A previous patient, a woman aged 68, had been seen on 18 May 1951 with a reddish lesion on the side of her nose, the size of a pea. This was considered clinically to be a pyogenic granuloma, and Dr. Haber reported: "Section represents a nodule covered by a thin atrophic epidermis. The corium is invaded by tumour masses which partly replace and partly displace the collagen. The tumour consists of masses of darkly staining nuclei with only a thin rim of protoplasm around them. The nuclei are mostly rounded but in places where they are compressed the nuclei appear spindle shaped. There are also many mitotic figures. Under the epidermis there are several dilated capillaries containing tumour cell emboli. Histology suggests secondary deposit of a tumour of unknown origin (? bronchus)."

The patient was very thoroughly investigated by Dr. S. Karani, and no abnormality was found. The patient was not seen after 20 November 1951, but enquiry was made of her general practitioner, and she was found to be in good health at present.

Dr. H. W. GORDON: A patient of mine was shown by Dr. Gold to the Society on 19 February 1953. The lesion was very similar, although it became slightly ulcerated. On two biopsies the pathologists could not be shaken that the lesion was a secondary carcinoma. Search for a primary was negative. The tumour was finally excised and to date the patient has remained completely well.

Dr. D. S. WILKINSON: I remember about two years ago a small cherry-red lesion diagnosed histologically as secondary carcinoma—possibly from the lung. The patient later developed glands in the axilla, but these were dealt with successfully. I looked up the records four months ago and the patient was then quite well. There is some peculiarity about these tumours.

An Unusual Case of Necrobiosis.—Dr. B. RUSSELL and Dr. H. HABER.

Mr. F. W.—, clerk aged 47.

History.—During the last 4 years he has noticed swellings on his chest which break down and leave scars. They cause discomfort in hot weather.

Present state.—On the front of the chest, on the left side more than on the right, are firm, button-like and annular, skin-coloured nodules and larger arciform, nodular areas with central scarring, yellow discoloration, and some ulceration and crusting. On the shoulders are discrete, skin-coloured nodules.

Mantoux test at 1:1000 strongly positive; 1:10,000 positive. Wassermann and Kahn reactions negative. Haemoglobin 106%. Total white blood cells 5200/c.mm. neutrophils 68%, eosinophils 1%, lymphocytes 28%, monocytes 3%. Fasting blood sugar 81 mg./100 ml. Blood cholesterol 168 mg./100 ml.

Histology.—The epidermis does not show any appreciable changes. Throughout the corium there is a widespread perivascular and periacinous infiltration of round cells, histiocytes, foam cells and foamy giant cells of the foreign body type. Stain for fat is positive. The cells are therefore xanthoma cells. The infiltrate is clearly related to partly degenerated collagen. The arrangement of histiocytes is that seen in granuloma annulare, but the presence of xanthoma cells is usually seen in necrobiosis lipoidica. The section represents therefore overlapping features of both conditions.

Treatment.—Two small areas have been treated with carbon dioxide snow and have become flat.

DR. BRIAN RUSSELL: This eruption is unusual whether one makes the diagnosis of granuloma annulare or of necrobiosis lipoidica. The age of the patient, the situation of the lesions, the necrotic, ulcerative and scarring changes with scaling, are all atypical of granuloma annulare. The situation of the lesions is also unusual for necrobiosis lipoidica. This patient seems to link these conditions, both clinically and histologically, because in the section there are overlapping features of both. Can it be that granuloma annulare and necrobiosis lipoidica are extreme examples of the same cutaneous reaction of unknown cause and that granuloma annulare has potentialities of recovery because it nearly always occurs in the young, whereas necrobiosis occurs in older persons, often diabetics with arteriosclerotic changes, and is irreversible?

Of the cases shown the following have been published in *Proc. R. Soc. Med.*, **47**, 173:

Porokeratosis Striata (Nekam).—Dr. H. MEARA (for Dr. J. E. M. WIGLEY).
Lymphangiosarcoma in Postmastectomy Lymphoedema (Stewart-Treves Syndrome).—Dr. S. P. HALL-SMITH and Dr. H. HABER.
Scleredema (Buschke).—Dr. C. D. CALNAN.

The following cases also were shown:

Pyodermite Végétante.—Dr. H. J. WALLACE.

Case for Diagnosis.—Dr. PETER BORRIE.

Naevoxanthoendothelioma.—Dr. E. LIPMAN COHEN.

(1) **Scleroderma—en Coup de Sabre.** (2) **Reiter's Disease.**—Dr. J. B. LYON.

OBITUARY

OLIVER SAMUEL ORMSBY,
1874-1954.

Dr. ORMSBY's passing climaxes the activities of over 50 years of clinical practice in Chicago. Dr. Ormsby was respected as one of the world's keenest and ablest dermatological diagnosticians, but remained always a profound student. This was well exemplified in his constructive teaching of medical students which resulted in the training of many able American dermatologists. As one of the founders of the Chicago Dermatological Society, he was a regular attendant and a most active participant in all of its endeavours. His accomplishments in the field of education are well known and will be only briefly alluded to here.

Dr. Ormsby was born on 21 March 1874 in Logan, Utah. He graduated from Rush Medical College, Chicago, in 1895 and was Chairman of the Department of Dermatology of the Rush Medical College from 1908 to 1944 when he became Emeritus Professor of Dermatology of the University of Illinois College of Medicine. He was certified by the American Board of Dermatology, and practised in Chicago since 1901.

Dr. Ormsby was the author of many fine articles, but is perhaps best known as author of *Practical Treatise on Diseases of the Skin*, with its many editions, which is so well recognized and accepted as the dermatologist's textbook.

Among his many activities, Dr. Ormsby was Chairman of the Section on Dermatology of the American Medical Association in 1920; Past-President of the Institute of Medicine of Chicago, and of the Chicago Dermatological Society. He has been an Honorary Member of the British Association of Dermatology since 1927. In 1951, he was elected Honorary Member of the American Dermatological Society and was also Honorary Member of the *Asociacion Argentina de Dermatologia y Sifilologia*, the *Wiener Dermatologische Gesellschaft*, the Japanese Dermatological Society, the Greek Union of Dermatology and Venereology and Hellenic Antivenereal Society. He was corresponding member of several international dermatological societies, including the Section of Dermatology of the Royal Society of Medicine of London, *Société française de Dermatologie et de Syphiligraphie*, Swedish Dermatological Society, *Deutsche Dermatologische Gesellschaft*, and the *Dansk Dermatologisk Selskab*. He was a member of all of the important societies in America, being one of the founders of the American Dermatological Association. As the outstanding teacher and dermatologist that he was, Dr. Ormsby exerted a tremendous influence on the development of dermatology as a speciality in Chicago, and maintained a notable influence throughout the world. In 1901 he joined the medical staff of the Presbyterian Hospital where he was head of the department for many years.

C. J. W.

THE BRITISH ASSOCIATION OF DERMATOLOGY.

THE Thirty-fourth Annual Meeting of the Association was held at Cambridge on 24, 25 and 26 June under the presidency of Dr. C. H. Whittle.

At the Business Meeting, with which the proceedings opened, the following Executive Committee was elected for the ensuing year :

President : Dr. B. C. Tate.

Hon. Treasurer : Sir Archibald Gray.

Hon. Secretary : Dr. G. B. Dowling.

Hon. Editor : Dr. F. R. Bettley.

Assistant Editor : Dr. G. W. Bamber.

Ordinary Members of the Executive Committee : Dr. G. A. Hodgson, Dr. I. Muende, Dr. G. A. Grant Peterkin, Dr. A. D. Porter, Dr. P. D. Samman, Dr. J. Sommerville, Dr. C. H. Whittle, Dr. J. E. M. Wigley, Dr. D. I. Williams.

It was agreed that the thirty-fifth Annual Meeting be held in Birmingham in 1955.

Dr. H. W. Barber and Dr. W. H. Brown were then elected Honorary Members. The following were elected Honorary Foreign Members : Professor Jean Gaté, Dr. P. V. Marcussen, Professor Stephen Rothman and Dr. Cleveland White.

The following Ordinary Members were elected : Dr. A. J. E. Barlow, Dr. R. J. Cairns, Dr. F. Glyn-Hughes, Dr. L. J. A. Loewenthal, Dr. J. A. Milne, Dr. J. Morgan, Dr. A. Aitken Ross.

A request was received for affiliation of the New Zealand Branch of the Association and this was unanimously agreed.

Finally, members were reminded of the deaths during the past year of Dr. Robert Aitken, Professor Dujardin, Dr. Guy Lane, Dr. Oliver Ormsby and Professor J. Schaumann.

The Scientific Meeting began with a discussion on "The Eczema-Asthma Syndrome with particular reference to Besnier's Prurigo." This was opened by Dr. J. T. Ingram, who was followed by Dr. Barbara Woodhead, Dr. Robert Warin, Dr. Ian Whimster, Dr. R. H. Meara and Dr. Brian Russell. These papers provoked a lively discussion which continued for the rest of the morning and was summarized after lunch. After this we heard papers from Dr. W. R. Bett (A Little Judicious Levity in Dermatology); Dr. P. J. Hare (Polydactyly); Dr. J. S. Pegum (Dissociated Depigmentation in Vitiligo); Dr. R. E. Church and Dr. W. Sircus (Recurrent Aphthous Stomatitis).

The next day we devoted the morning to a discussion on Patch Testing in which papers were read by Dr. S. C. Gold, Dr. C. D. Calnan, Dr. J. B. Lyon, Dr. H. T. H. Wilson and Dr. Brian Russell. In the time that remained towards the end of the morning Dr. A. W. Frankland read an interesting paper on "Some Allergic Responses to Insects." Friday afternoon was occupied by short papers: Dr. Daphne Anderson (Normal and Abnormal Keratinization); Dr. I. Magnus (Content of Thiols of Skin and Scales in certain Dermatoses); Dr. P. Montgomery (Skin Sensitivity due to Amalgam of Dental Fillings).

On Saturday morning there was a demonstration of thirty-three clinical cases of varied and considerable interest. Demonstrations were also arranged by Dr. A. Glucksmann (Local Factors in the Hypertrophy of Scars); Mr. J. L. Haybittle (Beta-ray Applicators using Cerium-144 and an Iridium-192 Teletherapy Unit); Dr. A. J. Rook and Dr. M. G. P. Stoker (The differential Diagnosis of Certain Virus Infections Transmitted from Animals to Man); Mr. P. H. Mortimer (Hyperkeratosis in the Bovine) and Mr. A. R. Jennings (So-Called Skin Tuberculosis in the Bovine). These cases and demonstrations were afterwards discussed until the meeting came to an end.

Members of the Association were charmingly entertained by Dr. and Mrs. Whittle on the lawns of Queen's College on Thursday evening. The Annual Dinner took place in the Hall of Trinity College on Friday evening; the principal speakers were Dr. H. J. Wallace who proposed the health of the guests and Professor Leslie Banks who replied; Dr. Alice Carleton who proposed the health of the Association and Dr. C. H. Whittle who replied. Dr. Douglas Freshwater was presented with the Golf Challenge Cup which he had wrested from the Scottish holder during the afternoon.

It has become almost traditional in recent years that we manage to hold our Annual Meeting during some of the finest part of the summer. Our Meeting at Cambridge lived nearly, though not quite, up to previous standards and we felt we were seeing the University and the City at its best. Dr. Whittle's decision to arrange the main discussions as a larger number of comparatively short papers was a very happy one and led to a very successful meeting. We all came away full of appreciation of our colleagues who had presented papers, of the work done by Dr. Whittle and his local secretary, Dr. Arthur Rook, and of the charming hospitality they had shown us.

BOOK REVIEW.

A HANDBOOK OF DISEASES OF THE SKIN.*

THIS book is intended primarily for students and it is therefore a tragedy that its main characteristic is a complete lack of discrimination between the common and the rare, the important and the unimportant. Thirteen pages are devoted to fungi and their pathological manifestations (although the student is not told what colour the microsporon fluoresces under Wood's light), whereas seborrhoeic dermatitis is dismissed in a page and a half in the appendix, pityriasis capitis and pruritus vulvae not being described at all. Thirty-one constitutional causes are listed for pruritus ani, but the deep veins are not mentioned in the discussion on the causes of "varicose ulcer," nor is one word given to the psychological aspect of infantile eczema. A "summary of recent literature" on the latter subject mentions, without comment, four papers, the first maintaining that fungi are the main causal agents, but the age at onset of the malady and its natural history are features that the student will have to discover for himself.

A general description of external and internal treatment covers eleven pages, but nowhere is it stated that granuloma annulare, strawberry naevi and warts resolve spontaneously. The only treatment advocated for warts is curettage and cautery and all forms of vascular naevi are dealt with by similar physical means. For descriptive purposes, eczema is divided into various morphological types, such as eczema madidans, eczema fissum, etc., and the student will find these dealt with in the chapter on industrial dermatitis. He will not, however, find nummular eczema, cheiropompholyx or atopic dermatitis dealt with anywhere.

The choice of illustrations also exemplifies this lack of critical selection. Six excellent photographs of urticaria pigmentosa do not compensate for the absence of any showing acne vulgaris, alopecia areata, haemangiomas, infantile eczema or warts.

The second characteristic of this book is the somewhat startling choice of treatments. "Sulphur ointment is the standard remedy" for scabies, and ultra-violet light when given for psoriasis should be "always kept just below an erythema dose." Whereas sulphapyridine is recommended for dermatitis herpetiformis, penicillin "given for a seven-day course" (dosage not stated) has, the student is told, superseded arsenic. For the treatment of acne vulgaris, "amongst the preparations used internally with success are thymus" etc., but oestrogens are not mentioned.

These examples of an unorthodox therapeutic approach, while doing little to equip the student to deal with his dermatological problems, are unlikely actively to harm his patients. This, unfortunately, cannot be said of vitamin A given in doses of 100,000 units daily for napkin rash, especially when it is not stated for how long the treatment should be continued. The same may be said of benzocaine being the first choice for topical anti-pruritic therapy. Finally "the standard method of treatment" for impetigo is stated to be either penicillin ointment or sulphadiazine cream and this régime is recommended also for sycosis barbae, bullous impetigo of infants and infected infantile eczema.

It is regretted that it is not possible to recommend this book to anyone anxious to learn the rudiments of dermatology, least of all students.

P. B.

* *A Handbook of Diseases of the Skin.* By H. O. MACKEY. 1954. London: MacMillan & Co. Ltd. Pp. 208 + xiv. Figs. 142. Price 7s. 6d.

HIRSUTISM.*

THE senior author of this small monograph is one of France's most distinguished endocrinologists and it is mainly from an endocrinological standpoint that he and his collaborators have studied the problem of hirsutism. Their conclusions are based on an exhaustive clinical and biochemical investigation of thirty patients and a thorough review of the literature.

Hirsutism is defined as an excessive growth of hair of normal distribution. In hypertrichosis the hair is of male distribution. In simple hypertrichosis feminine characters are otherwise retained. In hypertrichotic virilism (*virilisme pileaire*) there are associated android changes. Hypertrichosis also occurs in association with other syndromes, including Cushing's syndrome and acromegaly. Nine of the patients investigated were found to have Cushing's syndrome, 15 had simple hypertrichosis, and the remainder were examples of hypertrichotic virilism. The inevitably provisional nature of any classification is emphasized by the authors' patient who suffered from simple hypertrichosis from the age of 13 and developed Cushing's syndrome during her second pregnancy at the age of 36.

The results of the investigations are described in detail. Of considerable interest is the finding that abnormalities of glucose and insulin tolerance are common in simple hypertrichosis, as are disturbances of menstruation and a cycle of hyperoestrogenic type. There was no relationship between the level of 17-ketosteroid excretion and the severity of the hypertrichosis. Of practical importance is the observation that significant enlargement of the clitoris, long periods of amenorrhoea and a high level of 17-ketosteroid excretion were observed only in the presence of a malignant suprarrenal tumour. Ketosteroid excretion in excess of 50 mg. in 24 hours is suggestive of a tumour. This figure is considerably lower than that accepted by most authorities.

In discussing the aetiology of hypertrichosis the authors mention the importance of variations in tissue response to hormones, but insist that we are not yet in a position to draw definite conclusions about levels of hormonal secretion on the basis of the available facts which are almost restricted to measurements of urinary excretion.

Although certain of the biochemical sections are by no means easy reading for the average dermatologist the greater part of this useful little book can be read with interest and profit and there is a very full bibliography.

A. J. R.

A NEW FORMULARY.†

It is a well known fact that every dermatologist has his own favourite prescriptions, so that his pharmacopoeia for local applications usually differs considerably from that of each of his colleagues, and yet no doubt similar results are obtained. This formulary contains prescriptions which are, I am sure, used by few British specialists, but, as Drs. Frazier and Blank state, "no drug is included which is not in the U.S. Pharmacopoeia, the National Formulary, or in New and Non-official Remedies", and the prescriptions are "official on all clinical services throughout the Massachusetts General Hospital."

One looks in vain for tried favourites such as Lassar's paste and calamine liniment; instead, three main bases are recommended—"hydrated petrolatum", containing sorbitan sesquioleate, white petrolatum, methyl p-hydroxybenzoate and distilled

* *Hirsutism*. By M. Albeaux-Fernet, J. Robert and M. Caroit. Paris: Masson & Cie, 1954. Pp. 108. Illus. 11. Price 700 fr.

† *A Formulary for External Therapy of the Skin*. CHESTER N. FRAZIER and IRVIN H. BLANK (1954). Springfield, Illinois, U.S.A.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. Pp. 106. Price 23s. 6d.

water ; " emulsion base ", containing polyethylene glycol (200) monostearate, magnesium aluminium silicate, polysorbate 80, methyl p-hydroxybenzoate, and distilled water ; and " washable base ", with polyethylene glycol (200) monostearate, polyoxyethylene stearate and white petrolatum. To these bases are added powders such as starch or active medicaments as required. The reviewer, having almost entirely abandoned the use of water-miscible bases in eczematous conditions because of the frequency of undesirable reactions, wonders whether these three bases will be guiltless in this respect, considers how their cost will compare with other simpler bases, and doubts whether some of the ingredients will be available in this and other countries in the sterling area.

The logic and common-sense abounding in this slim book persuade one that these bases would not be recommended on flimsy or theoretical grounds, and that they have passed thorough practical tests. It pleases one to read that medicated soaps, with the exception of hexachlorophene, are useless ; that distilled and synthetic tars are not nearly so effective as crude coal tar ; and that, for the relief of itching in acute dermatoses, it is better to use cool or tepid water than chemicals such as Burow's solution, boric acid, saline or potassium permanganate.

This is not a book for the general practitioner, but can be warmly recommended to dermatologists who will find much to interest them, and who will enjoy, for example, the historical survey, in which one suspects the hand of Dr. Frazier, and the chapter on ointment vehicles, which one might attribute to Dr. Blank. G. A. G. P.

CORRESPONDENCE.

To the Editor of 'The British Journal of Dermatology.'

SIR,—The difficulty described in the report of a case of unilateral orbital pigmentation, of distinguishing between silver and melanin in histologic sections of skin (*Brit. J. Derm.*, 1954, **66**, 147) prompts me to remind the discussants of an old and apparently forgotten technique, which accomplishes this both simply and dramatically. I learned it some twenty years ago from Dr. James Mitchell of Chicago; but I am not aware that it has ever been published.



It consists simply of examining a skin section (preferably unstained) by dark-field illumination. The silver proteinate granules shine brilliantly at all magnifications, outlining the base of the epidermis, the appendages and most especially the sweat gland acini, in a most spectacular fashion, as the illustration shows.

Straub Clinic,
Honolulu, Hawaii.
19 May 1954.

I am, yours, etc.,
HARRY L. ARNOLD, Jr.